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(21) International Application Number: PCT/US99/00182 (22) International Filing Date: 14 January 1999 (14.01.99) (30) Priority Data: 60/071,374 15 January 1998 (15.01.98) US 60/093,491 20 July 1998 (20.07.98) US 60/110,941 4 December 1998 (04.12.98) US 09/232,197 14 January 1999 (14.01.99) US 09/232,200 14 January 1999 (14.01.99) US 09/232,201 14 January 1999 (14.01.99) US 09/232,195 14 January 1999 (14.01.99) US (71) Applicants (for all designated States except US): WHITE-HEAD INSTITUTE FOR BIOMEDICAL RESEARCH [US/US]; Nine Cambridge Center, Cambridge, MA 02142 (US). MILLENNIUM PHARMACEUTICALS, INC. [US/US]; 238 Main Street, Cambridge, MA 02142 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): STAHL, Andreas [DE/US]; 12 Farrington Avenue #2, Allston, MA 02134 (US). HIRSCH, David, J. [US/US]; 120 Amory Street #5, Brookline, MA 02146 (US). LODISH, Harvey, F. [US/US]; 195 Fischer Avenue, Brookline, MA 02146 (US). GIMENO, Ruth, E. [DE/US]; 65 Beverly Road, Wellesley,		MA 02481 (US). TARTAGLIA, Louis, A. [US/US]; 32 Manor House Road, Newton, MA 02159 (US). (74) Agents: GRANAHAN, Patricia et al.; Hamilton, Brook, Smith & Reynolds, P.C., Two Militia Drive, Lexington, MA 02421 (US). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>	
(54) Title: FATTY ACID TRANSPORT PROTEINS			
(57) Abstract			
<p>A family of fatty acid transport proteins (FATPs) mediate transport of long chain fatty acids (LCFAs) across cell membranes into cells. These proteins exhibit different expression patterns among the organs of mammals. Nucleic acids encoding FATPs of this family, vectors comprising these nucleic acids, as well as the production of FATP proteins in host cells are described. Also described are methods to test FATPs for fatty acid transport function, and methods to identify inhibitors or enhancers of transport function. The altering of LCFA uptake by administering to the mammal an inhibitor or enhancer of FATP transport function of a FATP in the small intestine can decrease or increase calories available as fats, and can decrease or increase circulating fatty acids. The organ specificity of FATP distribution can be exploited in methods to direct drugs, diagnostic indicators and so forth to an organ such as the heart.</p>			

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FATTY ACID TRANSPORT PROTEINS

RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application Number 60/071,374 entitled "Identification of a Family of Fatty Acid Transporters
5 Conserved From Mycobacterium to Man," by Andreas Stahl, David Hirsch and Harvey F. Lodish, filed on January 15, 1998; U.S. Provisional Application Number 60/093,491 entitled "Fatty Acid Transport Proteins," by Andreas Stahl, David J. Hirsch, Harvey F. Lodish, Ruth E. Gimeno and Louis A. Tartaglia, filed on July 20, 1998; and U.S. Provisional Application Number 60/110,941 entitled "Fatty Acid
10 Transport Proteins," by Andreas Stahl, David J. Hirsch, Harvey F. Lodish, Ruth E. Gimeno and Louis A. Tartaglia, filed on December 4, 1998. This application also claims priority to Attorney's Docket Nos. WHI97-21p3MA, WHI97-21p3MB, WHI97-21p3MC, WHI97-21p3MD, each of which is entitled "Fatty Acid Transport Proteins," by Andreas Stahl, David J. Hirsch, Harvey F. Lodish, Ruth E. Gimeno
15 and Louis A. Tartaglia, filed on January 14, 1999. The teachings of each of these referenced applications are incorporated herein by reference in their entirety.

GOVERNMENT SUPPORT

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20 The United States Government has certain rights in the invention.

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BACKGROUND OF THE INVENTION

Long chain fatty acids (LCFAs) are an important source of energy for most organisms. They also function as blood hormones, regulating key metabolic functions such as hepatic glucose production. Although LCFAs can diffuse through the hydrophobic core of the plasma membrane into cells, this nonspecific transport cannot account for the high affinity and specific transport of LCFAs exhibited by cells such as cardiac muscle, hepatocytes, enterocytes, and adipocytes. The molecular mechanisms of LCFA transport remains largely unknown. Identifying these mechanisms can lead to pharmaceuticals that modulate fatty acid uptake by the intestine and by other organs, thereby alleviating certain medical conditions (e.g. obesity).

SUMMARY OF THE INVENTION

Described herein is a diverse family of fatty acid transport proteins (FATPs) which are evolutionarily conserved; these FATPs are plasma membrane proteins which mediate transport of LCFAs across the membranes and into cells. Members of the FATP family described herein are present in a wide variety of organisms, from mycobacteria to humans, and exhibit very different expression patterns in tissues among the organisms. FATP family members are expressed in prokaryotic and eukaryotic organisms and comprise characteristic amino acid domains or sequences which are highly conserved across family members. In addition, the function of the FATP gene family is conserved throughout evolution, as shown by the fact that the *Caenorhabditis* (*C.*) *elegans* and mycobacterial FATPs described herein facilitate LCFA uptake when they are overexpressed in COS cells or *Escherichia* (*E.*) *coli*, respectively. FATPs are expressed in a wide variety of tissues, including all tissues which are important to fatty acid metabolism (uptake and processing).

In specific embodiments, FATPs of the present invention are from such diverse organisms as humans (*Homo* (*H.*) *sapiens*), mice, (*Mus* (*M.*) *musculus*), *F. rubripes*, *C. elegans*, *Drosophila* (*D.*) *melanogaster*, *Saccharomyces* (*S.*) *cerevisiae*, *Aspergillus*

nidulans, *Cochliobolu heterostrophus*, *Magnaporthe grisea* and *Mycobacterium (M.)*, such as *M. tuberculosis*. As described herein, four novel mouse FATPs, referred to as mmFATP2, mmFATP3, mmFATP4 and mmFATP5, and six human FATPs, referred to as hsFATP1, hsFATP2, hsFATP3, hsFATP4, hsFATP5 and hsFATP6, have been
5 identified. All four novel murine FATPs (mmFATP2-5) and a previously identified murine FATP (renamed herein FATP1) have orthologs in humans (hsFATP1-5); the sixth human FATP (hsFATP6) does not as yet have a mouse ortholog. The expression patterns of these FATPs vary, as described in detail below.

The present invention relates to FATP family members from prokaryotes and
10 eukaryotes, nucleic acids (DNA, RNA) encoding FATPs, and nucleic acids which are useful as probes or primers (e.g., for use in hybridization methods, amplification methods) for example, in methods of detecting FATP-encoding genes, producing FATPs, and purifying or isolating FATP-encoding DNA or RNA. Also the subject of this invention are antibodies (polyclonal or monoclonal) which bind an FATP or
15 FATPs; methods of identifying additional FATP family members (for example, orthologs of those FATPs described herein by amino acid sequence) and variant alleles of known FATP genes; methods of identifying compounds which bind to an FATP, or modulate or alter (enhance or inhibit) FATP function; compounds which modulate or alter FATP function; methods of modulating or altering (enhancing or inhibiting) FATP
20 function and, thus, LCFA uptake into tissues of a mammal (e.g. human) by administering a compound or molecule (a drug or agent) which increases or reduces FATP activity; and methods of targeting compounds to tissues by administering a complex of the compound to be targeted to tissues and a component which is bound by an FATP present on cells of the tissues to which the compound is to be targeted. For
25 example, a complex of a drug to be delivered to the liver and a component which is bound by an FATP present on liver cells (e.g., FATP5) can be administered.

In one embodiment, the present invention relates to modulating or altering (enhancing or inhibiting/reducing) LCFA uptake in the small intestine and, thus,

increasing or reducing the number of calories in the form of fats available to an individual. In another embodiment, the present invention relates to inhibiting or reducing LCFA uptake in the small intestine in order to reduce circulating fatty acid levels; that is, LCFA uptake in the small intestine is reduced and, therefore, circulating
5 (blood) levels are not as high as they otherwise would be. FATP4 has been shown to be expressed in epithelial cells of the small intestine and particularly in the brush border layer of the small intestine. FATP2 has also been shown to be expressed at low levels in epithelial cells of the small intestine, particularly in the duodenum. In contrast, FATP1, FATP3, FATP5 and FATP6 were not detected in any of the intestinal tissues.
10 Thus, also described herein are FATPs which are present in the epithelial cell layer of the small intestine where they mediate LCFA uptake. These FATPs, particularly FATP4 and also FATP2, are targets for methods and drugs which block their function or activity and are useful in treating obesity, diabetes and heart disease. The ability of these FATPs to mediate fat uptake can be modulated or altered (enhanced or inhibited),
15 thus modulating fat uptake in the small intestine. This can be done, for example, by administering to an individual, such as a human or other animal, a drug which blocks interaction of LCFAs with FATP4 and/or FATP2 in the small intestine, thus inhibiting LCFA passage into the cells of the small intestine. As a result, fat absorption is reduced and, although the individual has consumed a certain quantity of fat, the LCFAs are not
20 absorbed to the same extent they would have been in the absence of the compound administered.

Thus, one embodiment of this invention is a method of reducing LCFA uptake (absorption) in the small intestine and, as a result, reducing caloric uptake in the form of fat. A further embodiment is a compound (drug) useful in inhibiting or reducing fat
25 absorption in the small intestine. In another embodiment, the invention is a method of reducing circulating fatty acid levels by administering to an individual a compound which blocks interactions of LCFAs with FATP4 and/or FATP2 in the small intestine, thus inhibiting LCFA passage into cells of the small intestine. As a result, fatty acids

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pass into the circulatory system at a diminished level and/or rate, and circulating fatty acid levels are lower than they would be in the absence of the compound administered. This method is particularly useful for therapy in individuals who are at risk for or have hyperlipidemia. That is, it can be used to prevent the occurrence of elevated levels of lipids in the blood or to treat an individual in whom blood lipid levels are elevated. Also the subject of this invention is a method of identifying compounds which alter FATP function (and thus, in the case of FATP2 and/or FATP4, alter LCFA uptake in the small intestine).

In another embodiment, the present invention relates to a method of modulating or altering (enhancing or inhibiting) the function of FATP6, which is expressed at high levels in the heart. A method of inhibiting FATP6 function is useful, for example, in individuals with heart disease, such as ischemia, since reducing LCFA uptake into heart muscle in an individual who has ischemic heart disease, which may be manifested by, for example, angina or heart attack, can reduce symptoms or reduce the extent of damage caused by the ischemia. In this embodiment, a drug which inhibits FATP6 function is administered to an individual who has had or is having a heart attack, to reduce LCFA uptake by the individual's heart and, as a result, reduce the damage caused by ischemia. In a further embodiment, this invention is a method of targeting a compound, such as a therapeutic drug or an imaging reagent, to heart tissue by administering to an individual (e.g., a human) a complex of the compound and a component (e.g., a LCFA or LCFA-like compound) which is bound by an FATP (e.g., FATP6) present in cells of heart tissue.

In a further embodiment, LCFA uptake by the liver is modulated or altered (enhanced or reduced), in an individual. For example, a drug which inhibits the function of an FATP present in liver (e.g., FATP5) is administered to an individual who is diabetic, in order to reduce LCFA uptake by liver cells and, thus reduce insulin resistance.

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The present invention, thus, provides methods which are useful to alter, particularly reduce, LCFA uptake in individuals and, as a result, to alter (particularly reduce), availability of the LCFAs for further metabolism. In a specific embodiment, the present invention provides methods useful to reduce LCFA uptake and, thus, fatty acid metabolism in individuals, with the result that caloric availability from fats is reduced, and circulating fatty acid levels are lower than they otherwise would be. These methods are useful, for example, as a means of weight control in individuals, (e.g., humans) and as a means of preventing elevated serum lipid levels or reducing serum lipid levels in humans. FATPs expressed in the small intestine, such as FATP4, are useful targets to be blocked in treating obesity (e.g., chronic obesity) or to be enhanced in treating conditions in which enhanced LCFA uptake is desired (e.g., malabsorption syndrome or other wasting conditions).

The identification of this evolutionarily conserved fatty acid transporter family will allow a better understanding of the mechanisms whereby LCFAs traverse the lipid bilayer as well as yield insight into the control of energy homeostasis and its dysregulation in diseases such as diabetes and obesity.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows the amino acid sequence alignment of FATPs: mmFATP1 (SEQ ID NO:92), mmFATP2 (SEQ ID NO:93), mmFATP3 (SEQ ID NO:94), mmFATP4 (SEQ ID NO:95), mmFATP5 (SEQ ID NO:96), ceFATPa (SEQ ID NO:97), scFATP (SEQ ID NO:98) and mtFATP (SEQ ID NO:99). The underlining (amino acid residues 204-212 of mtFATP) indicates an AMP binding motif which is found in many classes of proteins; the underlining at amino acid residues 204-507 of the mtFATP sequence indicates the FATP 360 amino acid signature sequence.

Figures 2A-2D show results of LCFA uptake assays. Figures 2A-2D: COS cells were cotransfected using the DEAE-dextran method with the mammalian expression vectors pCDNA-CD2 either alone (control; Figure 2A) or in combination

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with one of the FATP-containing expression vectors (pCDNA-mmFATP1, Figure 2B; pCDNA-mmFATP2, Figure 2C; or pCMV-SPORT2-mmFATP5, Figure 2D) as described in Materials and Methods for Example 2. COS cells were gated on forward scatter (FSC) and side scatter (SS), and the results shown represent >10,000 cells. Cells
5 exhibiting >300 CD2 fluorescence units (vertical line) representing 15% of all cells were deemed CD2 positive.

Figure 3 is a graph of fluorescence of cells expressing a FATP gene. As in Figures 2A-2D, COS cells were cotransfected with pCDNA-CD2 either alone (control) or in combination with one of the FATP-containing expression vectors (pCDNA-
10 mmFATP1, pCDNA-mmFATP2, pCMV-SPORT2-mmFATP5, or pCDNA-ceFATPb). The mean BODIPY-FA fluorescence of the CD2-positive cells is plotted; results shown represent the average of three experiments, each consisting of greater than 50,000 COS cells. Note that a logarithmic scale is used on the ordinate.

Figure 4 is a graph of the uptake of palmitate with time. The full-length coding
15 region of mtFATP (squares) or a control protein (TFE3; circles) was subcloned into the inducible, prokaryotic expression vector pET (Novagen). Expression from the resulting plasmid was induced (solid symbols) in transformed *E. coli* cells with 1 mM isopropyl- β -D-thiogalactoside (IPTG) for 1 hour, or cells were left uninduced (open symbols). Data points were done in triplicate and counts were normalized to the number of
20 bacteria as determined by OD₆₀₀.

Figure 5 is a phylogenetic tree produced by aligning complete and partial sequences for *FATP* genes from human, rat, mouse, puffer fish, *D. melanogaster*, *C. elegans*, *S. cerevisiae*, and *M. tuberculosis* using ClustalX and using these data to produce a phylogenetic tree using TreeViewPPC. The bar indicates the number of
25 substitutions per residue, i.e., 0.1 corresponds to a distance of 10 substitutions per 100 residues.

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Figure 6 shows a comparison of the FATP signature sequences of mmFATP1. (SEQ ID NO:1), mmFATP5, (SEQ ID NO:2), ceFATPa (SEQ ID NO:3), scFATP (SEQ ID NO:4) and mtFATP (SEQ ID NO:5).

Figure 7 shows the sequence identity among the FATP family members and VLACs, based on the 360 amino acid signature sequence of FATP from Figure 1.

Figures 8A and 8B are the mmFATP3 DNA sequence (SEQ ID NO:6).

Figure 9 is the mmFATP3 protein sequence (SEQ ID NO:7).

Figures 10A and 10B are the mmFATP4 DNA sequence (SEQ ID NO:8).

Figure 11 is the mmFATP4 protein sequence (SEQ ID NO:9).

Figures 12A and 12B are the mmFATP5 DNA sequence (SEQ ID NO:10).

Figure 13 is the mmFATP5 protein sequence (SEQ ID NO:11).

Figures 14A and 14B are the hsFATP2 DNA sequence (SEQ ID NO:12).

Figure 15 is the hsFATP2 protein sequence (SEQ ID NO:13).

Figures 16A and 16B are the hsFATP3 DNA sequence (SEQ ID NO:14).

Figure 17 is the hsFATP3 protein sequence (SEQ ID NO:15).

Figures 18A and 18B are the hsFATP4 DNA sequence (SEQ ID NO:16).

Figure 19 is the hsFATP4 protein sequence (SEQ ID NO:17).

Figures 20A and 20B are the hsFATP5 DNA sequence (SEQ ID NO:18).

Figure 21 is the hsFATP5 protein sequence (SEQ ID NO:19).

Figures 22A and 22B are the hsFATP6 DNA sequence (SEQ ID NO:20).

Figure 23 is the hsFATP6 protein sequence (SEQ ID NO:21).

Figures 24A and 24B are the mtFATP DNA sequence (SEQ ID NO:22).

Figure 25 is the mtFATP protein sequence (SEQ ID NO:23).

Figure 26 shows the DNA sequence (SEQ ID NO:24) and predicted amino acid sequence (SEQ ID NO:25) of human FATP1.

Figure 27 shows the DNA sequence (SEQ ID NO:26) and predicted amino acid sequence (SEQ ID NO:27) of human FATP4.

Figure 28A is a hydrophobicity plot for hsFATP1, showing that it has multiple membrane-spanning domains.

Figure 28B is the amino acid composition of hsFATP1.

Figure 28C is a hydrophilicity plot for hsFATP1, made using the Kyte-Doolittle
5 method, averaging hydrophilicity values for 18 amino acid residues at a time.

Figure 29A is a hydrophobicity plot for hsFATP4, showing that it has multiple membrane-spanning domains.

Figure 29B is a listing of the amino acid composition of hsFATP4.

Figure 29C is a hydrophilicity plot for hsFATP4, made using the Kyte-Doolittle
10 method, averaging hydrophilicity values for 18 amino acid residues at a time.

Figures 30A and 30B show a comparison of the nucleotide sequence of human FATP1 (SEQ ID NO:28) and the nucleotide sequence of mouse FATP1 (SEQ ID NO:29).

Figures 31A and 31B show a comparison of the nucleotide sequence of human
15 FATP4 (SEQ ID NO:30) and the nucleotide sequence of mouse FATP4 (SEQ ID NO:31).

Figure 32 shows a comparison of the amino acid sequence of human FATP1 (SEQ ID NO:32) and the amino acid sequence of mouse FATP1 (SEQ ID NO:33). Shaded amino acid residues match the consensus sequence exactly

20 Figure 33 shows a comparison at the amino acid level of human FATP4 (SEQ ID NO:34) and mouse FATP4 (SEQ ID NO:35). Shaded amino acid residues match the consensus sequence exactly.

Figure 34 shows the nucleotide sequence (SEQ ID NO:36) and predicted amino acid sequence (SEQ ID NO:37) of hsFATP6.

25 Figure 35A is a hydrophobicity plot for hsFATP6, showing that it has multiple membrane-spanning domains.

Figure 35B is a listing of the amino acid composition of hsFATP6.

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Figure 35C is a hydrophilicity plot for hsFATP6, made using the Kyte-Doolittle method, averaging hydrophilicity values for 18 amino acid residues at a time.

Figure 36 shows an alignment of the amino acid sequences of hsFATP1 (SEQ ID NO:38), hsFATP4 (SEQ ID NO:39) and hsFATP6 (SEQ ID NO:40). Shaded amino acid residues match the consensus sequence exactly.

Figure 37 shows results of assessment of fatty acid uptake by human FATP1 and human FATP4. The percent of CD2-positive cells exhibiting a BODIPY-fluorescence of more than 300 arbitrary units is plotted for the three different conditions tested.

Figure 38 is a graph showing uptake of tritiated oleate, with time, by 293 cells transfected with either (diamonds) a plasmid for expression of human FATP4 or (squares) a control plasmid.

Figure 39 is an illustration of the amino acid sequences of human FATP4 (SEQ ID NO:41) and mouse FATP4 (SEQ ID NO:42) compared to human FATP1 (SEQ ID NO:43). Shown by underlining are the FATP consensus sequence (236-556 of hsFATP1) and the AMP-binding motif (246-254 of hsFATP1). The human FATPs were cloned by screening libraries with sequences from ESTs (expressed sequence tags). Mouse FATP4 was cloned by PCR using degenerate primers.

Figure 40 is a graph showing the uptake, with time, of tritiated oleate by mouse enterocytes in the presence of no oligonucleotide (squares), sense oligonucleotide (circles) or antisense oligonucleotide (diamonds).

Figure 41 is a bar graph showing uptake of tritiated oleate, by mouse enterocytes in the presence of various concentrations of antisense (solid bars), mismatch (stippled bars) or sense (lined bars) oligonucleotides.

Figure 42 is a bar graph showing uptake of tritiated oleate and uptake of ³⁵S-labeled methionine by mouse enterocytes to which were added no oligonucleotide, the antisense oligonucleotide, or the mismatch oligonucleotide.

Figure 43A is the nucleotide sequence of the gene encoding mouse FATP4 (SEQ ID NO:44).

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Figure 43B is the amino acid sequence of mouse FATP4 protein (SEQ ID NO:45).

Figures 44A, 44B, and 44C are the hsFATP1 DNA sequence (SEQ ID NO:46).
Coding region: 175-2115 (1941 nt).

5 Figure 45 is the hsFATP1 protein sequence (SEQ ID NO:47).

Figures 46A and 46B are the hsFATP2 DNA sequence (SEQ ID NO:48).
Coding region: 223-2085 (1863 nt).

Figure 47 is the hsFATP2 protein sequence (SEQ ID NO:49).

Figure 48 is the partial DNA sequence of hsFATP3 (SEQ ID NO:50). Coding
10 region: 1-993.

Figure 49 is the partial protein sequence of hsFATP3 (SEQ ID NO:51).

Figures 50A, 50B, and 50C are the hsFATP4 DNA sequence (SEQ ID NO:52).
Coding region: 208-2139 (1932 nt).

Figure 51 is the hsFATP4 protein sequence (SEQ ID NO:53).

15 Figure 52 is the hsFATP5 partial DNA sequence (SEQ ID NO:54). Coding
region: 1-1062.

Figure 53 is the hsFATP5 partial protein sequence (SEQ ID NO:55).

Figures 54A, 54B, and 54C are the hsFATP6 DNA sequence (SEQ ID NO:56).
Coding region: 643-2502 (1860 nt).

20 Figure 55 is the hsFATP6 protein sequence (SEQ ID NO:57).

Figures 56A, 56B, and 56C are the mFATP1 DNA sequence (m=*Rattus
norvegicus*; (SEQ ID NO:58). Coding region: 75-2015 (1941 nt).

Figure 57 is the mFATP1 protein sequence (SEQ ID NO:59).

Figure 58A, 58B, and 58C are the mFATP2 DNA sequence (SEQ ID NO:60).
25 Coding region: 795-2657 (1863 nt).

Figure 59 is the mFATP2 protein sequence (SEQ ID NO:61).

Figure 60A and 60B are the mFATP4 partial DNA sequence (SEQ ID NO:62).
Coding region: 1-1218.

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Figure 61 is the mFATP4 partial DNA sequence (SEQ ID NO:63).

Figure 62A, 62B, and 62C are the mmFATP1 DNA sequence (SEQ ID NO:64).

Coding region: 1-1944.

Figure 63 is the mmFATP1 protein sequence (SEQ ID NO:65).

5 Figures 64A and 64B are the mmFATP2 DNA sequence (SEQ ID NO:66).

Coding region: 121-1992 (1872 nt).

Figure 65 is the mmFATP2 protein sequence (SEQ ID NO:67).

Figures 66A and 66B are the mmFATP3 partial DNA sequence (SEQ ID NO:68). Coding region: 1-1830.

10 Figure 67 is the mmFATP3 partial protein sequence (SEQ ID NO:69).

Figures 68A, 68B, and 68C are the mmFATP4 DNA sequence (SEQ ID NO:70).

Coding region: 1-1932.

Figures 69 is the mmFATP4 protein sequence (SEQ ID NO:71).

Figures 70A and 70B are the mmFATP5 DNA sequence (SEQ ID NO:72).

15 Coding region: 60-2129.

Figure 71 is the mmFATP5 protein sequence (SEQ ID NO:73).

Figures 72A and 72B are the dmFATP partial DNA sequence (dm=*Drosophila melanogaster*; SEQ ID NO:74). Coding region: 1-1773.

Figures 73 is the dmFATP partial protein sequence (SEQ ID NO:75).

20 Figure 74 is the drFATP partial DNA sequence (dr=*Danio rerio*, zebrafish; SEQ ID NO:76) Coding region: 1-173.

Figure 75 is the drFATP partial protein sequence (SEQ ID NO:77).

Figure 76A and 76B are the ceFATPa DNA sequence (SEQ ID NO:78). Coding region: 1-1953.

25 Figure 77 is the ceFATPa protein sequence (SEQ ID NO:79).

Figures 78A and 78B are the ceFATPb DNA sequence (SEQ ID NO:80).

Coding region: 1-1968.

Figure 79 is the ceFATPb protein sequence (SEQ ID NO:81).

Figures 80A and 80B are the chFATP DNA sequence (SEQ ID NO:82; ch=*Cochliobolu heterostrophus*). Coding region: 1-1932.

Figure 81 is the chFATP protein sequence (SEQ ID NO:83).

Figure 82 is the anFATP partial protein sequence (an=*Aspergillus nidulans*;
5 SEQ ID NO:84). Coding region: 1-597.

Figure 83 is the anFATP partial protein sequence (SEQ ID NO:85).

Figure 84 is the mgFATP partial DNA sequence (mg= *Magnaporthe grisea*, rice blast; SEQ ID NO:86). Coding region: 1-522.

Figure 85 is the mgFATP partial protein sequence (SEQ ID NO:87).

10 Figures 86A and 86B are the scFATP DNA sequence (SEQ ID NO:88). Coding region: 1-1872.

Figure 87 is the scFATP protein sequence (SEQ ID NO:89).

Figures 88A and 88B are the mtFATP DNA sequence (SEQ ID NO:90).

Figure 89 is the mtFATP protein sequence (SEQ ID NO:91). Coding region: 1-
15 1794.

Figure 90 is a consensus sequence of the FATP signature sequence (SEQ ID NO:

100), based on 23 independent sequences aligned in ClustalX. The height of the bar at each amino acid residue position indicates the degree of conservation at that position.

20 Gaps have been inserted to maintain the strength of the alignment.

Figure 91 is a hydrophilicity plot for hsFATP2, made using the Kyte-Doolittle method, averaging hydrophilicity values for 18 amino acid residues at a time.

Figure 92 is a hydrophilicity plot for the hsFATP3 partial protein, made using the Kyte-Doolittle method, averaging hydrophilicity values for 18 amino acid residues
25 at a time.

Figure 93 is a hydrophilicity plot for the hsFATP5 partial protein, made using the Kyte-Doolittle method, averaging hydrophilicity values for 18 amino acid residues at a time.

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Figures 94A and 94B are a representation of the DNA sequence (SEQ ID NO:101) of the hsFATP5 gene, and the amino acid sequence (SEQ ID NO:102) of the hsFATP5 protein.

DETAILED DESCRIPTION OF THE INVENTION

5 As described herein, FATPs are a large evolutionarily conserved family of proteins that mediate the transport of LCFAs into cells. The family includes proteins which are conserved from mycobacteria to humans and exhibit very different expression patterns in tissues. Specific embodiments described include FATPs from mice, humans, nematodes, fungi and mycobacteria which have been shown to be functional LCFA
10 transporters. The term "fatty acid transport proteins" ("FATPs") as used herein, refers to the proteins described herein as FATP1, FATP2, FATP3, FATP4, FATP5 and FATP6, which have been described in one or more species of mammals, as well as mtFATP, ceFATP, scFATP, anFATP, mgFATP, and chFATP, and other proteins sharing at least about 50% amino acid sequence similarity, preferably at least about 60%
15 sequence similarity, more preferably at least about 70% sequence similarity, and still more preferably, at least about 80% sequence similarity, and most preferably, at least about 90% sequence similarity in the approximately 360 amino acid signature sequence. The approximately 360 amino acid FATP signature sequence is shown in Figure 1. The consensus sequence of the signature sequence is shown in Figure 90. The nomenclature
20 used herein to refer to FATPs includes a species-specific prefix (e.g., mm, *Mus musculus*; hs or h, *Homo sapiens* or human; mt *M. tuberculosis*; dm, *D. melanogaster*; ce, *C. elegans*; sc, *Saccharomyces cerevisiae*) and a number such that mammalian homologues in different species share the same number. For example, six human and five mouse *FATP* genes which are expressed in a variety of tissues are described herein
25 and are referred to, respectively, as hsFATP1-hsFATP6 and mmFATP1-mmFATP5; for example, hsFATP4 and mmFATP4 are the human and mouse orthologs.

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Expression patterns of human and mouse FATPs have been assessed and are described below. Briefly, results of these assessments show that FATP5 is a liver-specific gene. FATP2 is highly expressed in liver and kidney. Both of these proteins, as well as FATP4 and FATPs from nematodes and mycobacteria, have been shown to be functional LCFA transporters. Results have also shown that FATP4 mRNA is present at high levels in epithelial cells of two regions of the small intestine (the jejunum and ileum) and at lower, but significant, levels in a third region (the duodenum). They further showed that FATP2 mRNA is present in epithelial cells of the duodenum at a level similar to that of FATP4 mRNA levels, but is present at lower levels in the jejunum and ileum. FATP4 mRNA was absent from other cell types of the small intestine and no FATP4 mRNA could be detected in any cells of the colon. No signals above background could be detected for FATP1, FATP3 and FATP5 in any of the intestinal tissues. Thus, FATP4 is the major FATP in the mouse small intestine, which supports a major role for FATP4 (along with FATP2 to a lesser extent) in absorption of free fatty acids. hsFATP4 was clearly expressed in the jejunum and ileum; expression was absent in the stomach. This, too, is consistent with a major role for FATP4 in absorption of fatty acids in the human gut. Analysis of FATP expression in human tissues, also described in detail below, showed that hsFATP6, which has no mouse ortholog as yet, is expressed at high levels in the heart and at low levels in the placenta, but is undetectable in the other tissues assessed (Example 9). This is consistent with a major role for FATP6 in absorption of fatty acids in the heart.

Long chain fatty acids (LCFAs) are an important energy source for pro- and eukaryotes and are involved in diverse cellular processes, such as membrane synthesis, intracellular signaling, protein modification, and transcriptional regulation. In developed Western countries, human dietary lipids are mainly di- and triglycerides and account for approximately 40% of caloric intake (Weisburger, J. H. (1997) *J. Am. Diet. Assoc.* 97:S16-S23). These lipids are broken down into fatty acids and glycerol by pancreatic lipases in the small intestine (Chapus, C., Rovey, M., Sarda, L & Verger, R.

(1988) *Biochimie* 70:1223-34); LCFAs are then transported into brush border cells, where the majority is re-esterified and secreted into the lymphatic system as chylomicrons (Green, P.H. & Riley, J.W. (1981) *Aust. N.Z.J. Med.* 11:84-90). Fatty acids are liberated from lipoproteins by the enzyme lipoprotein lipase, which is bound to the luminal side of endothelial cells (Scow, R.O. & Blachette-Mackie, E.J. (1992) *Mol. Cell. Biochem* 116:181-191). "Free" fatty acids in the circulation are bound to serum albumin (Spector, A.A. (1984) *Clin. Physiol. Biochem* 2:123-134) and are rapidly incorporated by adipocytes, hepatocytes, and cardiac muscle cells. The latter derive 60-90% of their energy through the oxidation of LCFAs (Neely, J.F. Rovetto, M.J. & Oram, J.F. (1972) *Prog. Cardiovasc. Dis.* 15:289-329). Although saturable and specific uptake of LCFAs has been demonstrated for intestinal cells, hepatocytes, cardiac myocytes, and adipocytes, the molecular mechanisms of LCFA transport across the plasma membrane have remained controversial (Hui, T.Y. & Bernlohr, D.A. (1997) *Front. Biosci.* 15:d222-31-d231; Schaffer, J.E. & Lodish, H.F. (1995) *Trends Cardiovasc. Med.* 5:218-224). Described herein is a large family of highly homologous mammalian LCFA transporters which show wide expression, including in all tissues relevant to fatty acid metabolism. Further described are novel members of this family in other species, including mycobacterial and nematode FATPs which, like their mammalian counterparts, are functional fatty acid transporters.

20 The discovery of a diverse but highly homologous family of FATPs is reminiscent of the glucose transporter family. In a manner similar to the FATPs, the glucose transporters have very divergent patterns of tissue expression (McGowan, K.M., Long, S.D. & Pekala, P.H. (1995) *Pharmacol. Ther.* 66:465-505). The FATPs, like glucose transporters, may also differ in their substrate specificities, uptake kinetics, and
25 hormonal regulation (Thorens, B. (1996) *Am. J. Physiol.* 270:G541-G553). Indeed, the levels of fatty acids in the blood, like those of glucose, can be regulated by insulin and are dysregulated in diseases such as noninsulin-dependent diabetes and obesity (Boden, G. (1997) *Diabetes* 46:3-10). The underlying mechanisms for the regulation of free

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fatty acid concentrations in the blood are not understood, but could be explained by hormonal modulation of FATPs.

Insulin-resistance is thought to be the major defect in non insulin-dependent diabetes mellitus (NIDDM) and is one of the earliest manifestations of NIDDM

5 (McGarry (1992) *Science* 258:766-770). Free fatty acids (FFAs) may provide an explanation for why obesity is a risk factor for NIDDM. Plasma levels of FFAs are elevated in diabetic patients (Reaven *et al.* (1988) *Diabetes* 37:1020). Elevated plasma free fatty acids (FFAs) have been demonstrated to induce insulin-resistance in whole animals and humans (Boden (1998) *Front. Biosci.* 3:D169-D175). This insulin-

10 resistance is likely mediated by effects of FFAs on a variety of issues. FFAs added to adipocytes *in vitro* induce insulin resistance in this cell type as evidenced by inhibition of insulin-induced glucose transport (Van Epps-Fung *et al.* (1997) *Endocrinology* 138:4338-4345). Rats fed a high fat diet developed skeletal muscle insulin resistance as evidenced by a decrease in insulin-induced glucose uptake by skeletal muscle (Han *et*

15 *al.*, (1997) *Diabetes* 46:1761-1767). In addition, elevated plasma FFAs increase insulin-suppressed endogenous glucose production in the liver (Boden (1998) *Front. Biosci.* 3:D169-D175), thus increasing hepatic glucose output. It has been postulated that the adverse effects of plasma free fatty acids are due to the FFAs being taken up into the cell, leading to an increase in intracellular long chain fatty acyl CoA;

20 intracellular long chain acyl CoAs are thought to mediate the effects of FFAs inside the cell. Thus, fatty acid induced insulin-resistance may be prevented by blocking uptake of FFAs into select tissues, in particular liver (by blocking FATP2 and/or FATP5), adipocyte (by blocking FATP1), and skeletal muscle (by blocking FATP1). Blocking intestinal fat absorption (by blocking FATP4) is also expected to reduce plasma FFA

25 levels and thus improve insulin resistance.

During the pathogenesis of NIDDM insulin-resistance can initially be counteracted by increasing insulin output by the pancreatic beta cell. Ultimately, this compensation fails, beta cell function decreases and overt diabetes results (McGarry

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(1992) *Science* 258: 766-770). Manipulating beta cell function is a second point where fatty acid transporter blockers may be beneficial for diabetes. While no FATP homolog has been identified so far that is expressed in the beta cell of the pancreas, the data described below suggest the existence of such a transporter and the sequence

5 information included herein provides the means to identify such a transporter by degenerate PCR, using primers to regions conserved in all FATP family members or by low stringency hybridization. It has been demonstrated that exposure of pancreatic beta-cells to FFAs increases the basal rate of insulin secretion; this in turn leads to a decrease in the intracellular stores of insulin, resulting in decreased capacity for insulin

10 secretion after chronic exposure (Bollheimer *et al.*, (1998) *J. Clin. Invest.* 101:1094-1101). The effects of FFAs are again likely to be mediated by intracellular long chain fatty acyl CoA molecules (Liu *et al.*, (1998) *J. Clin. Invest.* 101:1870-1875). FFAs have also been demonstrated to increase beta cell apoptosis (Shimabukuro *et al.*, (1998) *Proc. Nat. Acad. Sci. USA* 95:2498-2502), possibly contributing to the decrease in beta

15 cell numbers in late stage NIDDM.

Another finding with potentially broad implications is the identification of a FATP homologue in *M. tuberculosis*. Tuberculosis causes more deaths worldwide than any other infectious agent and drug-resistant tuberculosis is re-emerging as a problem in industrialized nations (Bloom, B.R. & Small, P.M. (1998) *N. Engl. J. Med.* 338:677-

20 678). *Mycobacterium tuberculosis* has about 250 enzymes involved in fatty acid metabolism, compared with only about 50 in *E. coli*. It has been suggested that, living as a pathogen, the mycobacteria are largely lipolytic, rather than lipogenic, relying on the lipids within mammalian cells and the tubercle (Cole, S.T. *et al.*, *Nature* 393:537-544 (1998)). The *de novo* synthesis of fatty acids in *Mycobacterium leprae* is

25 insufficient to maintain growth (Wheeler, P.R., Bulmer, K & Ratledge, C. (1990) *J. Gene. Microbiol.* 136:211-217). Thus, it is reasonable to expect that inhibitors of mtFATP will serve as therapeutics for tuberculosis. FATPs expressed in mycobacteria can be targeted to reduce or prevent replication of mycobacteria (e.g., to reduce or

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prevent replication of *M. tuberculosis*) and, thus, reduce or prevent their adverse effects. For example, a FATP or FATPs expressed by *M. tuberculosis* can be targeted and inhibited, thus reducing or preventing growth of this pathogen (and tuberculosis in humans and other mammals). An inhibitor of an *M. tuberculosis* FATP can be
5 identified, using methods described herein (e.g., expressing the FATP in an appropriate host cell, such as *E. coli* or COS cells; contacting the cells with an agent or drug to be assessed for its ability to inhibit the FATP and, as a result, mycobacterial growth, and assessing its effects on growth). A drug or agent identified in this manner can be further tested for its ability to inhibit a *M. tuberculosis* FATP and *M. tuberculosis* infection in
10 an appropriate animal model or in humans. A method of inhibiting mycobacterial growth, particularly growth of *M. tuberculosis*, and compounds useful as drugs for doing so are also the subject of this invention.

An isolated polynucleotide encoding mtFATP, like other polynucleotides encoding FATPs of the FATP family, can be incorporated into vectors, nucleic acids of
15 viruses, and other nucleic acid constructs that can be used in various types of host cells to produce mtFATP. This mtFATP can be used, as it appears on the surface of cells, or in various artificial membrane systems, to assess fatty acid transport function, to identify ligands and molecules that are modulators of fatty acid transport activity. Molecules found to be inhibitors of mtFATP function can be incorporated into
20 pharmaceutical compositions to administer to a human for the treatment of tuberculosis.

Particular embodiments of the invention are polynucleotides encoding a FATP of *Cochliobolus (Helminthosporium) heterostrophus* or portions or variants thereof, the isolated or recombinantly produced FATP, methods for assessing whether an agent binds to the chFATP, and further methods for assessing the effect of an agent being
25 tested for its ability to modulate fatty acid transport activity. *Cochliobolus heterostrophus* is an ascomycete that is the cause of southern corn leaf blight, an economically important threat to the corn crop in the United States. The related species *C. sativus* causes crown rot and common root rot in wheat and barley. One or more

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FATPs of *C. heterostrophus* can be targeted for the identification of an inhibitor of chFATP function, which can be then be used as an agent effective against infection of plants by *C. heterostrophus* and related organisms. Methods described herein that were applied in studying the expression of a FATP gene and the function of the FATP in its natural site of expression or in a host cell, can be used in the study of the chFATP gene and protein.

Magnaporthe grisea (rice blast) is an economically important fungal pathogen of rice. Further embodiments of the invention are nucleic acid molecules encoding a FATP of *Magnaporthe grisea*, portions thereof, or variants thereof, isolated mgFATP, nucleic acid constructs, and engineered cells expressing mgFATP. Other aspects of the invention are assays to identify an agent which binds to mgFATP and assays to identify an agent which modulates the function of mgFATP in cells in which mgFATP is expressed or in artificial membrane systems. Agents identified as inhibiting mgFATP activity can be developed into anti-fungal agents to be used to treat rice infected with rice blast.

Caenorhabditis elegans is a nematode related to plant pathogens and human parasites. An isolated polynucleotide which encodes ceFATP, like other polynucleotides encoding FATPs of the FATP family described herein, can be incorporated into nucleic acid vectors and other constructs that can be used in various types of cells to produce ceFATP. ceFATP as it occurs in cells or as it can be isolated or incorporated into various artificial or reconstructed membrane systems, can be used to assess fatty acid transport, and to identify ligands and agents that modulate fatty acid transport activity. Agents found by such assays to be inhibitors of ceFATP activity can be incorporated into compositions for the treatment of diseases caused by genetically related organisms with a FATP of similar sensitivity to the agents.

Aspergillus nidulans is one of a family of fungal species that can infect humans. Further embodiments of the invention of the family of polynucleotides encoding FATPs are polynucleotides encoding a FATP of *Aspergillus nidulans*, and vectors and host

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cells that can be constructed to comprise such polynucleotides. Further embodiments are a polypeptide encoded by such polynucleotides, portions thereof having one or more functions characteristic of a FATP, and various methods. The methods include those for identifying agents that bind to anFATP and those for assessing the effect of an agent
5 being tested for its ability to modulate fatty acid transport activity. Those agents found to inhibit fatty acid transport function can be used in compositions as anti-fungal pharmaceuticals, or can be modified for greater effectiveness as a pharmaceutical.

One aspect of the invention relates to isolated nucleic acids that encode a FATP as described herein, such as those FATPs having an amino acid sequence in Figure 45
10 (SEQ ID NO:47), Figure 47 (SEQ ID NO:49), Figure 49 (SEQ ID NO:51), Figure 51 (SEQ ID NO:53), Figures 94A and 94B (SEQ ID NO:102), and Figure 55 (SEQ ID NO:57) and nucleic acids closely related thereto as described herein.

Using the information provided herein, such as a nucleic acid sequence set forth in Figures 44A-44C (SEQ ID NO:46), Figures 46A and 46B (SEQ ID NO:48), Figure
15 48 (SEQ ID NO:50), Figures 50A-50C (SEQ ID NO:52), Figures 94A and 94B (SEQ ID NO:101), and Figures 54A-54C (SEQ ID NO:56), a nucleic acid of the invention encoding a FATP polypeptide may be obtained using standard cloning and screening methods, such as those for cloning and sequencing cDNA library fragments, followed by obtaining a full length clone. For example, to obtain a nucleic acid of the invention,
20 a library of clones of cDNA of human or other mammalian DNA can be probed with a labeled oligonucleotide, such as a radiolabeled oligonucleotide, preferably about 17 nucleotides or longer, derived from a partial sequence. Clones carrying DNA identical to that of the probe can then be distinguished using stringent (also, "high stringency") hybridization conditions. By sequencing the individual clones thus identified with
25 sequencing primers designed from the original sequence it is then possible to extend the sequence in both directions to determine the full length sequence. Suitable techniques are described, for example, in *Current Protocols in Molecular Biology* (F.M. Ausubel et

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al, eds), containing supplements through Supplement 42, 1998, John Wiley and Sons, Inc., especially chapters 5, 6 and 7.

Embodiments of the invention include isolated nucleic acid molecules comprising any of the following nucleotide sequences: 1.) a nucleotide sequence which
5 encodes a protein comprising the amino acid sequence of hsFATP1 (SEQ ID NO:47), the amino acid sequence of hsFATP2 (SEQ ID NO:49), the amino acid sequence of hsFATP3 (SEQ ID NO:51), the amino acid sequence of hsFATP4 (SEQ ID NO: 53), the amino acid sequence of hsFATP5 (SEQ ID NO:102) or the amino acid sequence of hsFATP6 (SEQ ID NO:57); 2.) nucleotide sequences of hsFATP1, hsFATP2,
10 hsFATP3, hsFATP4, hsFATP5, or hsFATP6 (SEQ ID NO:46, 48, 50, 52, 101, or 56, respectively); 3.) a nucleotide sequence which is complementary to the nucleotide sequence of hsFATP1 (SEQ ID NO:46), hsFATP2 (SEQ ID NO:48), hsFATP3 (SEQ ID NO:50), hsFATP4 (SEQ ID NO:52), hsFATP5 (SEQ ID NO:101) or hsFATP6 (SEQ ID NO:56); 4.) a nucleotide sequence which consists of the coding region of hsFATP1
15 (SEQ ID NO:46), the coding region of hsFATP2 (SEQ ID NO:48), the coding region of hsFATP3 (SEQ ID NO:50), the coding region of hsFATP4 (SEQ ID NO:52), the coding region of hsFATP5 (SEQ ID NO:101), or the coding region of hsFATP6 (SEQ ID NO:56).

The invention further relates to nucleic acids (nucleic acid molecules or
20 polynucleotides) having nucleotide sequences identical over their entire length to those shown in the figures, for instance Figures 44A-44C (SEQ ID NO:46), Figures 46A and 46B (SEQ ID NO:48), Figure 48 (SEQ ID NO:50), Figures 50A-50C (SEQ ID NO:52), Figures 94A and 94B (SEQ ID NO:101), and Figures 54A-54C (SEQ ID NO:56). It further relates to DNA, which due to the degeneracy of the genetic code, encodes a
25 FATP encoded by one of the FATP-encoding DNAs, whose amino acid sequence is provided herein. Also provided by the invention are nucleic acids having the coding sequences for the mature polypeptides or fragments in reading frame with other coding sequences, such as those encoding a leader or secretory sequence, a pre-, or pro- or

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prepro- protein sequence. The nucleic acids of the invention encompass nucleic acids that include a single continuous region or discontinuous regions encoding the polypeptide, together with additional regions, that may also contain coding or non-coding sequences. The nucleic acids may also contain non-coding sequences, including, for example, but not limited to, non-coding 5' and 3' sequences, such as the transcribed, non-translated sequences, termination signals, ribosome binding sites, sequences that stabilize mRNA, introns, polyadenylation signals, and additional coding sequences which encode additional amino acids. For example, a marker sequence that facilitates purification of the fused polypeptide can be encoded. In certain embodiments of the invention, the marker sequence can be a hexa-histidine peptide, as provided in the pQE vector (Qiagen, Inc.) and described in Gentz *et al.*, *Proc. Natl. Acad. Sci. USA* 86: 821-824 (1989), or an HA tag (Wilson *et al.*, *Cell* 37: 767 (1984)), or a sequence encoding glutathione S-transferase of *Schistosoma japonicum* (vectors available from Pharmacia; see Smith, D.B. and Johnson K.S., *Gene* 67:31 (1988) and Kaelin, W.G. *et al.*, *Cell* 70:351 (1992)). Nucleic acids of the invention also include, but are not limited to, nucleic acids comprising a structural gene and its naturally associated sequences that control gene expression.

The invention further relates to variants, including naturally-occurring allelic variants, of those nucleic acids described specifically herein by DNA sequence, that encode variants of such polypeptides as those having the amino acid sequences shown in Figure 45 (SEQ ID NO:47), Figure 47 (SEQ ID NO:49), Figure 49 (SEQ ID NO:51), Figure 51 (SEQ ID NO:53) Figures 94A and 94B (SEQ ID NO:102), or Figure 55 (SEQ ID NO:57). Such variants include nucleic acids encoding variants of the above-listed amino acid sequences, wherein those variants have several, such as 5 to 10, 1 to 5, or 3, 2 or 1 amino acids substituted, deleted, or added, in any combination. Variants include polynucleotides encoding polypeptides with at least 95% but less than 100% amino acid sequence identity to the polypeptides described herein by amino acid sequence. Variant polynucleotides hybridize, under low to high stringency conditions, to the alleles

described herein by DNA sequence. In one embodiment, variants have silent substitutions, additions and deletions that do not alter the properties and activities of the FATP. Allelic variants of the polynucleotides encoding hsFATP1 (Figure 45; SEQ ID NO:47), hsFATP2 (Figure 47; SEQ ID NO:49), hsFATP3 (Figure 49; SEQ ID NO:51),
5 hsFATP4 (Figure 51; SEQ ID NO:53), Figures 94A and 94B (SEQ ID NO:102) and hsFATP6 (Figure 55; SEQ ID NO:57) will be identified as mapping to chromosomal locations listed for the corresponding wild type genes in Table 2 in Example 1.

Orthologous genes are gene loci in different species that are sufficiently similar to each other in their nucleotide sequences to suggest that they originated from a
10 common ancestral gene. Orthologous genes arise when a lineage splits into two species, rather than when a gene is duplicated within a genome. Proteins that are orthologs are encoded by genes of two different species, wherein the genes are said to be orthologous.

The invention further relates to polynucleotides encoding polypeptides which are orthologous to those polypeptides having a specific amino acid sequence described
15 herein, such as the amino acid sequences shown in Figure 45 (SEQ ID NO:47), Figure 47 (SEQ ID NO:49), Figure 49 (SEQ ID NO:51), Figure 51 (SEQ ID NO:53), Figures 94A and 94B (SEQ ID NO:102), or Figure 55 (SEQ ID NO:57). These polynucleotides, which can be called ortholog polynucleotides, encode orthologous polypeptides that can range in amino acid sequence identity to a reference amino acid sequence described
20 herein, from about 65% to less than 100%, but preferably 70% to 80%, more preferably 80% to 90%, and still more preferably 90% to less than 100%. Orthologous polypeptides can also be those polypeptides that range in amino acid sequence similarity to a reference amino acid sequence described herein from about 75% to 100%, within the signature sequence. The amino acid sequence similarity between the signature
25 sequences of orthologous polypeptides is preferably 80%, more preferably 90%, and still more preferably, 95%. The ortholog polynucleotides encode polypeptides that have similar functional characteristics (e.g., fatty acid transport activity) and similar tissue

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distribution, as appropriate to the organism from which the ortholog polynucleotides can be isolated.

Ortholog polynucleotides can be isolated from (e.g., by cloning or nucleic acid amplification methods) a great number of species, as shown by the sample of FATPs
5 from evolutionarily divergent species described herein (see, e.g., Figures 44A-C through Figure 89). Ortholog polynucleotides corresponding to those in Figure 45 (SEQ ID NO:47), Figure 47 (SEQ ID NO:49), Figure 49 (SEQ ID NO:51), Figure 51 (SEQ ID NO:53), Figures 94A and 94B (SEQ ID NO:102) and Figure 55 (SEQ ID NO:57) are those which can be isolated from mammals such as rat, dog, chimpanzee, monkey,
10 baboon, pig, rabbit and guinea pig, for example.

Further variants that are fragments of the nucleic acids of the invention may be used to synthesize full-length nucleic acids of the invention, such as by use as primers in a polymerase chain reaction. As used herein, the term primer refers to a single-stranded oligonucleotide which acts as a point of initiation of template-directed DNA synthesis
15 under appropriate conditions (e.g., in the presence of four different nucleoside triphosphates and an agent for polymerization, such as DNA or RNA polymerase or reverse transcriptase) in an appropriate buffer and at a suitable temperature. The appropriate length of a primer depends on the intended use of the primer, but typically ranges from 15 to 30 nucleotides. Short primer molecules generally require cooler
20 temperatures to form sufficiently stable hybrid complexes with the template. A primer need not reflect the exact sequence of the template, but must be sufficiently complementary to hybridize with a template. The term primer site refers to the area of the target DNA to which a primer hybridizes. The term primer pair refers to a set of primers including a 5' (upstream) primer that hybridizes with the 5' end of the DNA
25 sequence to be amplified and a 3' (downstream) primer that hybridizes with the complement of the 3' end of the sequence to be amplified.

Further embodiments of the invention are nucleic acids that are at least 80% identical over their entire length to a nucleic acid described herein, for example a

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nucleic acid having the nucleotide sequence in Figures 44A-44C (SEQ ID NO:46), Figures 46A-46B (SEQ ID NO:48), Figure 48 (SEQ ID NO:50), Figures 50A-50C (SEQ ID NO:52), Figures 94A and 94B (SEQ ID NO:101), and Figures 54A-54C (SEQ ID NO:56). Additional embodiments are nucleic acids, and the complements of such
5 nucleic acids, having at least 90% nucleotide sequence identity to the above-described sequences, and nucleic acids having at least 95% nucleotide sequence identity. In preferred embodiments, DNA of the present invention has 97% nucleotide sequence identity, 98% nucleotide sequence identity, or at least 99% nucleotide sequence identity with the DNA whose sequences are presented herein.

10 Other embodiments of the invention are nucleic acids that are at least 80% identical in nucleotide sequence to a nucleic acid encoding a polypeptide having an amino acid sequence as set forth in Figure 45 (SEQ ID NO:47), Figure 47 (SEQ ID NO:49), Figure 49 (SEQ ID NO:51), Figure 51 (SEQ ID NO:53), Figures 94A and 94B (SEQ ID NO:102) or Figure 55 (SEQ ID NO:57), or as such amino acid sequences are
15 set forth elsewhere herein, and nucleic acids that are complementary to such nucleic acids. Specific embodiments are nucleic acids having at least 90% nucleotide sequence identity to a nucleic acid encoding a polypeptide having an amino acid sequence as described in the list above, nucleic acids having at least 95% sequence identity, and nucleic acids having at least 97% sequence identity.

20 The terms "complementary" or "complementarity" as used herein, refer to the natural binding of polynucleotides under permissive salt and temperature conditions by base-pairing. Complementarity between two single-stranded molecules may be "partial" in which only some of the nucleic acids bind, or it may be complete when total complementarity exists between the single-stranded molecules (that is, when A-T and
25 G-C base pairing is 100% complete). The degree of complementarity between nucleic acid strands has significant effects on the efficiency and strength of hybridization between nucleic acid strands. This is of particular importance in amplification reactions, which depend on binding between nucleic acid strands.

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The invention further includes nucleic acids that hybridize to the above-described nucleic acids, especially those nucleic acids that hybridize under stringent hybridization conditions. "Stringent hybridization conditions" or "high stringency conditions" generally occur within a range from about T_m minus 5°C (5° C below the strand dissociation temperature or melting temperature (T_m) of the probe nucleic acid molecule) to about 20° C to 25° C below T_m . As will be understood by those of skill in the art, the stringency of hybridization may be altered in order to identify or detect molecules having identical or related polynucleotide sequences. An example of high stringency hybridization follows. Hybridization solution is (6x SSC/10 mM EDTA/0.5% SDS/5x Denhardt's solution/100 µg/ml sheared and denatured salmon sperm DNA). Hybridization is at 64-65°C for 16 hours. The hybridized blot is washed two times with 2x SSC/0.5% SDS solution at room temperature for 15 minutes each, and two times with 0.2x SSC/0.5% SDS at 65°C, for one hour each. Further examples of high stringency conditions can be found on pages 2.10.1-2.10.16 (see particularly 2.10.8-11) and pages 6.3.1-6 in *Current Protocols in Molecular Biology* (Ausubel, F.M. *et al.*, eds., containing supplements up through Supplement 42, 1998). Examples of high, medium, and low stringency conditions can be found on pages 36 and 37 of WO 98/40404, which are incorporated herein by reference.

The invention further relates to nucleic acids obtainable by screening an appropriate library with a probe having a nucleotide sequence such as that set forth in Figures 44A-44C (SEQ ID NO:46), Figures 46A-46B (SEQ ID NO:48), Figure 48 (SEQ ID NO:50), Figures 50A-50C (SEQ ID NO:52), Figures 94A and 94B (SEQ ID NO:101) or Figures 54A-54C (SEQ ID NO:56), or a probe which is a sufficiently long fragment of any of the above; and isolating the nucleic acid. Such probes generally can comprise at least 15 nucleotides. Nucleic acids obtainable by such screenings may include RNAs, cDNAs and genomic DNA, for example, encoding FATPs of the FATP family described herein.

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Further uses for the nucleic acid molecules of the invention, whether encoding a full-length FATP or whether comprising a contiguous portion of a nucleic acid molecule such as one given in SEQ ID NO:46, 48, 50, 52, 101, or 56, include use as markers for tissues in which the corresponding protein is preferentially expressed (to identify

5 constitutively expressed proteins or proteins produced at a particular stage of tissue differentiation or stage of development of a disease state); as molecular weight markers on southern gels; as chromosome markers or tags (when labeled, for example with biotin, a radioactive label or a fluorescent label) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in a mammal to

10 identify potential genetic disorders; as probes to hybridize and thus identify, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel nucleic acid molecules; for selecting and making oligomers for attachment to a "gene chip" or other support, to be used, for example, for examination

15 of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or to elicit another immune response.

Further methods to obtain nucleic acids encoding FATPs of the FATP family include PCR and variations thereof (e.g., "RACE" PCR and semi-specific PCR

20 methods). Portions of the nucleic acids having a nucleotide sequence set forth in Figures 44A-44C (SEQ ID NO:46), Figures 46A-46B (SEQ ID NO:48), Figure 48 (SEQ ID NO:50), Figures 50A-50C (SEQ ID NO:52), Figures 94A and 94B (SEQ ID NO:101) or Figures 54A-54C (SEQ ID NO:56), (especially "flanking sequences" on either side of a coding region) can be used as primers in methods using the polymerase

25 chain reaction, to produce DNA from an appropriate template nucleic acid.

Once a fragment of the FATP gene is generated by PCR, it can be sequenced, and the sequence of the product can be compared to other DNA sequences, for example, by using the BLAST Network Service at the National Center for Biotechnology

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Information. The boundaries of the open reading frame can then be identified using semi-specific PCR or other suitable methods such as library screening. Once the 5' initiator methionine codon and the 3' stop codon have been identified, a PCR product encoding the full-length gene can be generated using genomic DNA as a template, with
5 primers complementary to the extreme 5' and 3' ends of the gene or to their flanking sequences. The full-length genes can then be cloned into expression vectors for the production of functional proteins.

The invention also relates to isolated proteins or polypeptides such as those encoded by nucleic acids of the present invention. Isolated proteins can be purified
10 from a natural source or can be made recombinantly. Proteins or polypeptides referred to herein as "isolated" are proteins or polypeptides that exist in a state different from the state in which they exist in cells in which they are normally expressed in an organism, and include proteins or polypeptides obtained by methods described herein, similar methods or other suitable methods, and also include essentially pure proteins or
15 polypeptides, proteins or polypeptides produced by chemical synthesis or by combinations of biological and chemical methods, and recombinant proteins or polypeptides which are isolated. Thus, the term "isolated" as used herein, indicates that the polypeptide in question exists in a physical milieu distinct from that in which it occurs in nature. Thus, "isolated" includes existing in membrane fragments and vesicles
20 membrane fractions, liposomes, lipid bilayers and other artificial membrane systems. An isolated FATP may be substantially isolated with respect to the complex cellular milieu in which it naturally occurs, and may even be purified essentially to homogeneity, for example as determined by PAGE or column chromatography (for example, HPLC), but may also have further cofactors or molecular stabilizers, such as
25 detergents, added to the purified protein to enhance activity. In one embodiment, proteins or polypeptides are isolated to a state at least about 75% pure; more preferably at least about 85% pure, and still more preferably at least about 95% pure, as determined by Coomassie blue staining of proteins on SDS-polyacrylamide gels. Proteins or

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polypeptides referred to herein as "recombinant" are proteins or polypeptides produced by the expression of recombinant nucleic acids.

In a preferred embodiment, an isolated polypeptide comprising a FATP, a functional portion thereof, or a functional equivalent of the FATP, has at least one function characteristic of a FATP, for example, transport activity, binding function (e.g., a domain which binds to AMP), or antigenic function (e.g., binding of antibodies that also bind to a naturally-occurring FATP, as that function is found in an antigenic determinant). Functional equivalents can have activities that are quantitatively similar to, greater than, or less than, the reference protein. These proteins include, for example, naturally occurring FATPs that can be purified from tissues in which they are produced (including polymorphic or allelic variants), variants (e.g., mutants) of those proteins and/or portions thereof. Such variants include mutants differing by the addition, deletion or substitution of one or more amino acid residues, or modified polypeptides in which one or more residues are modified, and mutants comprising one or more modified residues. Portions or fragments of a FATP can range in size from four amino acid residues to the entire amino acid sequence minus one amino acid.

The isolated proteins of the invention preferably include mammalian fatty acid transport proteins of the FATP family of homologous proteins. In one embodiment, the extent of amino acid sequence similarity between a polypeptide having one of the amino acid sequences shown in Figure 45 (SEQ ID NO:47), Figure 47 (SEQ ID NO:49), Figure 49 (SEQ ID NO:51), Figure 51 (SEQ ID NO:53), Figures 94A and 94B (SEQ ID NO:102), or Figure 55 (SEQ ID NO:57), and the respective functional equivalents of these polypeptides is at least about 88%. In other embodiments, the degree of amino acid sequence similarity between a FATP and its respective functional equivalent is at least about 91%, at least about 94%, or at least about 97%.

The polypeptides of the invention also include those FATPs encoded by polynucleotides which are orthologous to those polynucleotides, the sequences of which are described herein in whole or in part. FATPs which are orthologs to those described

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herein by amino acid sequence, in whole or in part, are, for example fatty acid transport proteins 1-6 of dog, rat chimpanzee, monkey, rabbit, guinea pig, baboon and pig, and are also embodiments of the invention.

To determine the percent identity or similarity of two amino acid sequences or
5 of two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment, and non-homologous (dissimilar) sequences can be disregarded for comparison purposes). In a preferred embodiment, the length of a reference sequence aligned for comparison purposes is at least 30%,
10 preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, and even more preferably at least 70%, 80%, or 90% of the length of the reference sequence. The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding
15 position in the second sequence, then the molecules are identical at that position (as used herein, amino acid or nucleic acid "identity" is equivalent to amino acid or nucleic acid "similarity"). The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment
20 of the two sequences.

The invention also encompasses polypeptides having a lower degree of identity but having sufficient similarity so as to perform one or more of the same functions performed by the polypeptides described herein by amino acid sequence. Similarity for a polypeptide is determined by conserved amino acid substitution. Such substitutions
25 are those that substitute a given amino acid in a polypeptide by another amino acid of like characteristics. Conservative substitutions are likely to be phenotypically silent. Typically seen as conservative substitutions are the replacements, one for another, among the aliphatic amino acids Ala, Val, Leu, and Ile; interchange of the hydroxyl

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residues Ser and Thr, exchange of the acidic residues Asp and Glu, substitution between the amide residues Asn and Gln, exchange of the basic residues Lys and Arg and replacements among the aromatic residues Phe, Tyr. Guidance concerning which amino acid changes are likely to be phenotypically silent is found in Bowie *et al.*, *Science*

5 247:1306-1310 (1990).

TABLE 1. Conservative Amino Acid Substitutions

	Aromatic		Phenylalanine	
			Tryptophan	
			Tyrosine	
	Hydrophobic		Leucine	
			Isoleucine	
			Valine	
	Polar		Glutamine	
			Asparagine	
5	Basic		Arginine	
			Lysine	
			Histidine	
	Acidic		Aspartic Acid	
			Glutamic Acid	
	Small		Alanine	
			Serine	
			Threonine	
			Methionine	
			Glycine	

The comparison of sequences and determination of percent identity and similarity between two sequences can be accomplished using a mathematical algorithm.

10 (Computational Molecular Biology, Lesk, A.M., ed., Oxford University Press, New York, 1988; Biocomputing: Informatics and Genome Projects, Smith, D.W., ed., Academic Press, New York, 1993; Computer Analysis of Sequence Data, Part 1, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, 1994; Sequence

Analysis in Molecular Biology, von Heinje, G., Academic Press, 1987; and *Sequence Analysis Primer*, Gribskov, M. and Devereaux, J., eds., M. Stockton Press, New York, 1991). In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (*J. Mol. Biol.* 5 (48):444-453 (1970)) algorithm which has been incorporated into the GAP program in the GCG software package (available at <http://www.gcg.com>), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the 10 GCG software package (Devereux, J., *et al.*, *Nucleic Acids Res.* 12(1):387 (1984)) (available at <http://www.gcg.com>), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. In another embodiment, the percent identity between two amino acid or nucleotide sequences is determined using the algorithm of E. Meyers and W. Miller (*CABIOS*, 4:11-17 (1989)) 15 which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

The nucleic acid and protein sequences of the present invention can further be used as a "query sequence" to perform a search against databases to, for example, identify other family members or related sequences. Such searches can be performed 20 using the NBLAST and XBLAST programs (version 2.0) of Altschul, *et al.* (*J. Mol. Biol.* 215:403-10 (1990)). BLAST nucleotide searches can be performed with the NBLAST program, score = 100, word length = 12 to obtain nucleotide sequences homologous to (with calculatably significant similarity to) the nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST program, 25 score = 50, word length = 3 to obtain amino acid sequences homologous to the proteins of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul *et al.*, (*Nucleic Acids Res.* 25(17):3389-3402 (1997)). When utilizing BLAST and gapped BLAST programs, the default

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parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See <http://www.ncbi.nlm.nih.gov>.

Similarity for nucleotide and amino acid sequences can be defined in terms of the parameters set by the Advanced Blast search available from NCBI (the National Center for Biotechnology Information; see, for Advanced BLAST page, www.ncbi.nlm.nih.gov/cgi-bin/BLAST/nph-newblast?Jform=1). These default parameters, recommended for a query molecule of length greater than 85 amino acid residues or nucleotides have been set as follows: gap existence cost, 11, per residue gap cost, 1; lambda ratio, 0.85. Further explanation of version 2.0 of BLAST can be found on related website pages and in Altschul, S.F. *et al.*, *Nucleic Acids Res.* 25:3389-3402 (1997).

The invention further relates to fusion proteins, comprising a FATP or functional portion thereof (as described above) as a first moiety, linked to second moiety not occurring in the FATP as found in nature. Thus, the second moiety can be an amino acid, peptide or polypeptide. The first moiety can be in an N-terminal location, C-terminal location or internal to the fusion protein. In one embodiment, the fusion protein comprises a FATP as the first moiety, and a second moiety comprising a linker sequence and an affinity ligand. Fusion proteins can be produced by a variety of methods. For example, a fusion protein can be produced by the insertion of a FATP gene or portion thereof into a suitable expression vector, such as Bluescript SK +/- (Stratagene), pGEX-4T-2 (Pharmacia), pET-24(+) (Novagen), or vectors of similar construction. The resulting construct can be introduced into a suitable host cell for expression. Upon expression, fusion protein can be purified from cells by means of a suitable affinity matrix (See e.g., *Current Protocols in Molecular Biology*, Ausubel, F.M. *et al.*, eds., Vol. 2, pp. 16.4.1-16.7.8, containing supplements up through Supplement 42, 1998).

The invention also relates to enzymatically produced, synthetically produced, or recombinantly produced portions of a fatty acid transport protein. Portions of a FATP

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can be made which have full or partial function on their own, or which when mixed together (though fully, partially, or nonfunctional alone), spontaneously assemble with one or more other polypeptides to reconstitute a functional protein having at least one function characteristic of a FATP.

5 Fragments of a FATP can be produced by direct peptide synthesis, for example those using solid-phase techniques (Roberge, J.Y. *et al.*, *Science* 269:202-204 (1995); Merrifield, J., *J. Am. Chem. Soc.* 85:2149-2154 (1963)). Protein synthesis can be performed using manual techniques or by automation. Automated synthesis can be carried out using, for instance, an Applied Biosystems 431A Peptide Synthesizer
10 (Perkin Elmer). Various fragments of a FATP can be synthesized separately and combined using chemical methods.

One aspect of the invention is a peptide or polypeptide having the amino acid sequence of a portion of a fatty acid transport protein which is hydrophilic rather than hydrophobic, and ordinarily can be detected as facing the outside of the cell membrane.
15 Such a peptide or polypeptide can be thought of as being an extracellular domain of the FATP, or a mimetic of said extracellular domain. It is known, for example, that a portion of human FATP4 that includes a highly conserved motif is involved in AMP-CoA binding function (Stuhlsatz-Krouper, S.M. *et al.*, *J. Biol. Chem.* 44:28642-28650 (1998)).

20 The term "mimetic" as used herein, refers to a molecule, the structure of which is developed from knowledge of the structure of the FATP of interest, or one or more portions thereof, and, as such, is able to effect some or all of the functions of a FATP.

Portions of an FATP can be prepared by enzymatic cleavage of the isolated protein, or can be made by chemical synthesis methods. Portions of a FATP can also be
25 made by recombinant DNA methods in which restriction fragments, or fragments that may have undergone further enzymatic processing, or synthetically made DNAs are joined together to construct an altered FATP gene. The gene can be made such that it encodes one or more desired portions of a FATP. These portions of FATP can be

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entirely homologous to a known FATP, or can be altered in amino acid sequence relative to naturally occurring FATPs to enhance or introduce desired properties such as solubility, stability, or affinity to a ligand. A further feature of the gene can be a sequence encoding an N-terminal signal peptide directed to the plasma membrane.

5 An extracellular domain can be determined by a hydrophobicity plot, such as those shown in Figures 28A, 29A, and 35A, or by a hydrophilicity plot such as those shown in Figures 28C, 29C, 35C, 91, 92 and 93. A polypeptide or peptide comprising all or a portion of a FATP extracellular domain can be used in a pharmaceutical composition. When administered to a mammal by an appropriate route, the polypeptide
10 or peptide can bind to fatty acids and compete with the native FATPs in the membrane of cells, thereby making fewer fatty acid molecules available as substrates for transport into cells, and reducing the amount of fatty acids taken up by, for example, the heart, in the case of FATP6.

 Another aspect of the invention relates to a method of producing a fatty acid
15 transport protein, variants or portions thereof, and to expression systems and host cells containing a vector appropriate for expression of a fatty acid transport protein.

 Cells that express a FATP, a variant or a portion thereof, or an ortholog of a FATP described herein by amino acid sequence, can be made and maintained in culture, under conditions suitable for expression, to produce protein in the cells for cell-based
20 assays, or to produce protein for isolation. These cells can be procaryotic or eucaryotic. Examples of procaryotic cells that can be used for expression include *Escherichia coli*, *Bacillus subtilis* and other bacteria. Examples of eucaryotic cells that can be used for expression include yeasts such as *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Pichia pastoris* and other lower eucaryotic cells, and cells of higher eucaryotes
25 such as those from insects and mammals, such as primary cells and cell lines such as CHO, HeLa, 3T3 and BHK cells, preferably COS cells and human kidney 293 cells, and more preferably Jurkat cells. (See, e.g., Ausubel, F.M. *et al.*, eds. *Current Protocols in*

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Molecular Biology, Greene Publishing Associates and John Wiley & Sons, Inc., containing Supplements up through Supplement 42, 1998)).

In one embodiment, host cells that produce a recombinant FATP, or a portion thereof, a variant, or an ortholog of a FATP described herein by amino acid sequence, can be made as follows. A gene encoding a FATP, variant or a portion thereof can be
5 inserted into a nucleic acid vector, e.g., a DNA vector, such as a plasmid, phage, cosmid, phagemid, virus, virus-derived vector (e.g., SV40, vaccinia, adenovirus, fowl pox virus, pseudorabies viruses, retroviruses) or other suitable replicon, which can be present in a single copy or multiple copies, or the gene can be integrated in a host cell
10 chromosome. A suitable replicon or integrated gene can contain all or part of the coding sequence for a FATP or variant, operably linked to one or more expression control regions whereby the coding sequence is under the control of transcription signals and linked to appropriate translation signals to permit translation. The vector can be introduced into cells by a method appropriate to the type of host cells (e.g.,
15 transfection, electroporation, infection). For expression from the FATP gene, the host cells can be maintained under appropriate conditions (e.g., in the presence of inducer, normal growth conditions, etc.). Proteins or polypeptides thus produced can be recovered (e.g., from the cells, as in a membrane fraction, from the periplasmic space of bacteria, from culture medium) using suitable techniques. Appropriate membrane
20 targeting signals may be incorporated into the expressed polypeptide. These signals may be endogenous to the polypeptide or they may be heterologous signals.

Polypeptides of the invention can be recovered and purified from cell cultures (or from their primary cell source) by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography,
25 phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and high performance liquid chromatography. Known methods for refolding protein can be used to regenerate active conformation if the polypeptide is denatured during isolation or purification.

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In a further aspect of the invention are methods for assessing the transport function of any of the fatty acid transport proteins or polypeptides described herein, including orthologs, and in variations of these, methods for identifying an inhibitor (or an enhancer) of such function and methods for assessing the transport function in the presence of a candidate inhibitor or a known inhibitor.

A variety of systems comprising living cells can be used for these methods. Cells to be used in fatty acid transport assays, and further in methods for identifying an inhibitor or enhancer of this function, express one or more FATPs. See Examples 3, 6, 9, 12 and 14 for data on tissue distribution of expression of FATPs, and Examples 10 and 11 describing recombinant cells expressing FATP. Cells for use in cell-based assays described herein can be drawn from a variety of sources, such as isolated primary cells of various organs and tissues wherein one or more FATPs are naturally expressed. In some cases, the cells can be from adult organs, and in some cases, from embryonic or fetal organs, such as heart, lung, liver, intestine, skeletal muscle, kidney and the like. Cells for this purpose can also include cells cultured as fragments of organs or in conditions simulating the cell type and/or tissue organization of organs, in which artificial materials may be used as substrates for cell growth. Other types of cells suitable for this purpose include cells of a cell strain or cell line (ordinarily comprising cells considered to be "transformed") transfected to express one or more FATPs.

A further embodiment of the invention is a method for detecting, in a sample of cells, a fatty acid transport protein, a portion or fragment thereof, a fusion protein comprising a FATP or a portion thereof, or an ortholog as described herein, wherein the cells can be, for instance, cells of a tissue, primary culture cells, or cells of a cell line, including cells into which nucleic acid has been introduced. The method comprises adding to the sample an agent that specifically binds to the protein, and detecting the agent specifically bound to the protein. Appropriate washing steps can be added to reduce nonspecific binding to the agent. The agent can be, for example, an antibody, a ligand or a substrate mimic. The agent can have incorporated into it, or have bound to

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it, covalently or by high affinity non-covalent interactions, for instance, a label that facilitates detection of the agent to which it is bound, wherein the label can be, but is not limited to, a phosphorescent label, a fluorescent label, a biotin or avidin label, or a radioactive label. The means of detection of a fatty acid transport protein can vary, as appropriate to the agent and label used. For example, for an antibody that binds to the fatty acid transport protein, the means of detection may call for binding a second antibody, which has been conjugated to an enzyme, to the antibody which binds the fatty acid transport protein, and detecting the presence of the second antibody by means of the enzymatic activity of the conjugated enzyme.

10 Similar principles can also be applied to a cell lysate or a more purified preparation of proteins from cells that may comprise a fatty acid transport protein of interest, for example in the methods of immunoprecipitation, immunoblotting, immunoaffinity methods, that in addition to detection of the particular FATP, can also be used in purification steps, and qualitative and quantitative immunoassays. See, for instance, chapters 11 through 14 in *Antibodies: A Laboratory Manual*, E. Harlow and D. Lane, eds., Cold Spring Harbor Laboratory, 1988.

Isolated fatty acid transport protein or, an antigenically similar portion thereof, especially a portion that is soluble, can be used in a method to select and identify molecules which bind specifically to the FATP. Fusion proteins comprising all of, or a portion of, the fatty acid transport protein linked to a second moiety not occurring in the FATP as found in nature, can be prepared for use in another embodiment of the method. Suitable fusion proteins for this purpose include those in which the second moiety comprises an affinity ligand (e.g., an enzyme, antigen, epitope). FATP fusion proteins can be produced by the insertion of a gene encoding the FATP or a variant thereof, or a suitable portion of such gene into a suitable expression vector, which encodes an affinity ligand (e.g., pGEX-4T-2 and pET-15b, encoding glutathione S-transferase and His-Tag affinity ligands, respectively). The expression vector can be introduced into a suitable host cell for expression. Host cells are lysed and the lysate, containing fusion

protein, can be bound to a suitable affinity matrix by contacting the lysate with an affinity matrix.

In one embodiment, the fusion protein can be immobilized on a suitable affinity matrix under conditions sufficient to bind the affinity ligand portion of the fusion protein to the matrix, and is contacted with one or more candidate binding agents (e.g., a mixture of peptides) to be tested, under conditions suitable for binding of the binding agents to the FATP portion of the bound fusion protein. Next, the affinity matrix with bound fusion protein can be washed with a suitable wash buffer to remove unbound candidate binding agents and non-specifically bound candidate binding agents. Those agents which remain bound can be released by contacting the affinity matrix with fusion protein bound thereto with a suitable elution buffer. Wash buffer can be formulated to permit binding of the fusion protein to the affinity matrix, without significantly disrupting binding of specifically bound binding agents. In this aspect, elution buffer can be formulated to permit retention of the fusion protein by the affinity matrix, but can be formulated to interfere with binding of the candidate binding agents to the target portion of the fusion protein. For example, a change in the ionic strength or pH of the elution buffer can lead to release of specifically bound agent, or the elution buffer can comprise a release component or components designed to disrupt binding of specifically bound agent to the target portion of the fusion protein.

Immobilization can be performed prior to, simultaneous with, or after, contacting the fusion protein with candidate binding agent, as appropriate. Various permutations of the method are possible, depending upon factors such as the candidate molecules tested, the affinity matrix-ligand pair selected, and elution buffer formulation. For example, after the wash step, fusion protein with binding agent molecules bound thereto can be eluted from the affinity matrix with a suitable elution buffer (a matrix elution buffer, such as glutathione for a GST fusion). Where the fusion protein comprises a cleavable linker, such as a thrombin cleavage site, cleavage from the affinity ligand can release a portion of the fusion with the candidate agent bound

thereto. Bound agent molecules can then be released from the fusion protein or its cleavage product by an appropriate method, such as extraction.

One or more candidate binding agents can be tested simultaneously. Where a mixture of candidate binding agents is tested, those found to bind by the foregoing processes can be separated (as appropriate) and identified by suitable methods (e.g.,
5 PCR, sequencing, chromatography). Large libraries of candidate binding agents (e.g., peptides, RNA oligonucleotides) produced by combinatorial chemical synthesis or by other methods can be tested (see e.g., Ohlmeyer, M.H.J. *et al.*, *Proc. Natl. Acad. Sci. USA* 90:10922-10926 (1993) and DeWitt, S.H. *et al.*, *Proc. Natl. Acad. Sci. USA*
10 90:6909-6913 (1993), relating to tagged compounds; see also Rutter, W.J. *et al.* U.S. Patent No. 5,010,175; Huebner, V.D. *et al.*, U.S. Patent No. 5,182,366; and Geysen, H.M., U.S. Patent No. 4,833,092). Random sequence RNA libraries (see Ellington, A.D. *et al.*, *Nature* 346:818-822 (1990); Bock, L.C. *et al.*, *Nature* 355:584-566 (1992); and Szostak, J.W., *Trends in Biochem. Sci.* 17:89-93 (March, 1992)) can also be
15 screened according to the present method to select RNA molecules which bind to a target FATP or FATP fusion protein. Where binding agents selected from a combinatorial library by the present method carry unique tags, identification of individual biomolecules by chromatographic methods is possible. Where binding agents do not carry tags, chromatographic separation, followed by mass spectrometry to
20 ascertain structure, can be used to identify binding agents selected by the method, for example.

The invention also comprises a method for identifying an agent which inhibits interaction between a fatty acid transport protein (e.g., one comprising the amino acid sequence in SEQ ID NO:47, SEQ ID NO:49, SEQ ID NO:51, SEQ ID NO:53, SEQ ID
25 NO:102, or SEQ ID NO:57), and a ligand of said protein. The FATP can be one described by amino acid sequence herein, a portion or fragment thereof, a variant thereof, or an ortholog thereof, or a FATP fusion protein. Here, a ligand can be, for instance, a substrate, or a substrate mimic, an antibody, or a compound, such as a

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peptide, that binds with specificity to a site on the protein. The method comprises combining, not limited to a particular order, the fatty acid protein, the ligand of the protein, and a candidate agent to be assessed for its ability to inhibit interaction between the protein and the ligand, under conditions appropriate for interaction between the protein and the ligand (e.g., pH, salt, temperature conditions conducive to appropriate conformation and molecular interactions); determining the extent to which the protein and ligand interact; and comparing (1) the extent of protein-ligand interaction in the presence of candidate agent with (2) the extent of protein-ligand interaction in the absence of candidate agent, wherein if (1) is less than (2), then the candidate agent is one which inhibits interaction between the protein and the ligand.

The method can be facilitated, for example, by using an experimental system which employs a solid support (column chromatography matrix, wall of a plate, microtiter wells, column pore glass, pins to be submerged in a solution, beads, etc.) to which the protein can be attached. Accordingly, in one embodiment, the protein can be fixed to a solid phase directly or indirectly, by a linker. The candidate agent to be tested is added under conditions conducive for interaction and binding to the protein. The ligand is added to the solid phase system under conditions appropriate for binding. Excess ligand is removed, as by a series of washes done under conditions that do not disrupt protein-ligand interactions. Detection of bound ligand can be facilitated by using a ligand that carries a label (e.g., fluorescent, chemiluminescent, radioactive). In a control experiment, protein and ligand are allowed to interact in the absence of any candidate agent, under conditions otherwise identical to those used for the "test" conditions where candidate inhibiting agent is present, and any washes used in the test conditions are also used in the control. The extent to which ligand binds to the protein in the presence of candidate agent is compared to the extent to which ligand binds to the protein in the absence of the candidate agent. If the extent to which interaction of the protein and the ligand occurs is less in the presence of the candidate agent than in the

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absence of the candidate agent, the candidate agent is an agent which inhibits interaction between the protein and the ligand of the protein.

In a further embodiment, an inhibitor (or an enhancer) of a fatty acid transport protein can be identified. The method comprises steps which are, or are variations of the following: contacting the cells with fatty acid, wherein the fatty acid can be labeled for convenience of detection; contacting a first aliquot of the cells with an agent being tested as an inhibitor (or enhancer) of fatty acid uptake while maintaining a second aliquot of cells under the same conditions but without contact with the agent; and measuring (e.g., quantitating) fatty acid in the first and second aliquots of cells; wherein a lesser quantity of fatty acid in the first aliquot compared to that in the second aliquot is indicative that the agent is an inhibitor of fatty acid uptake by a fatty acid transport protein. A greater quantity of fatty acid in the first aliquot compared to that in the second aliquot is indicative that the agent is an enhancer of fatty acid uptake by a fatty acid transport protein.

A particular embodiment of identifying an inhibitor or enhancer of fatty acid transport function employs the above steps, but also employs additional steps preceding those given above: introducing into cells of a cell strain or cell line ("host cells" for the intended introduction of, or after the introduction of, a vector) a vector comprising a fatty acid transport protein gene, wherein expression of the gene can be regulatable or constitutive, and providing conditions to the host cells under which expression of the gene can occur.

The terms "contacting" and "combining" as used herein in the context of bringing molecules into close proximity to each other, can be accomplished by conventional means. For example, when referring to molecules that are soluble, contacting is achieved by adding the molecules together in a solution. "Contacting" can also be adding an agent to a test system, such as a vessel containing cells in tissue culture.

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The term "inhibitor" or "antagonist", as used herein, refers to an agent which blocks, diminishes, inhibits, hinders, limits, decreases, reduces, restricts or interferes with fatty acid transport into the cytoplasm of a cell, or alternatively and additionally, prevents or impedes the cellular effects associated with fatty acid transport. The term

5 "enhancer" or "agonist", as used herein, refers to an agent which augments, enhances, or increases fatty acid transport into the cytoplasm of a cell. An antagonist will decrease fatty acid concentration, fatty acid metabolism and byproduct levels in the cell, leading to phenotypic and molecular changes.

In order to produce a "host cell" type suitable for fatty acid uptake assays and for

10 assays derived therefrom for identifying inhibitors or enhancers thereof, a nucleic acid vector can be constructed to comprise a gene encoding a fatty acid transport protein, for example, human FATP1, FATP2, FATP3, FATP4, FATP5, FATP6, a mutant or variant thereof, an ortholog of the human proteins, such as mouse orthologs or orthologs found in other mammals, or a FATP family protein of origin in an organism other than a

15 mammal. The gene of the vector can be regulatable, such as by the placement of the gene under the control of an inducible or repressible promoter in the vector (e.g., inducible or repressible by a change in growth conditions of the host cell harboring the vector, such as addition of inducer, binding or functional removal of repressor from the cell milieu, or change in temperature) such that expression of the FATP gene can be

20 turned on or initiated by causing a change in growth conditions, thereby causing the protein encoded by the gene to be produced, in host cells comprising the vector, as a plasma membrane protein. Alternatively, the FATP gene can be constitutively expressed.

A vector comprising an FATP gene, such as a vector described herein, can be

25 introduced into host cells by a means appropriate to the vector and to the host cell type. For example, commonly used methods such as electroporation, transfection, for instance, transfection using CaCl_2 , and transduction (as for a virus or bacteriophage) can be used. Host cells can be, for example, mammalian cells such as primary culture cells

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- or cells of cell lines such as COS cells, 293 cells or Jurkat cells. Host cells can also be, in some cases, cells derived from insects, cells of insect cell lines, bacterial cells, such as *E. coli*, or yeast cells, such as *S. cerevisiae*. It is preferred that the fatty acid transport protein whose function is to be assessed, with or without a candidate inhibitor or
- 5 enhancer, be produced in host cells whose ancestor cells originated in a species related to the species of origin of the FATP gene encoding the fatty acid transport protein. For example, it is preferable that tests of function or of inhibition or enhancement of a mammalian FATP be carried out in host mammalian cells producing the FATP, rather than bacterial cells or yeast cells.
- 10 Host cells comprising a vector comprising a regulatable FATP gene can be treated so as to allow expression of the FATP gene and production of the encoded protein (e.g., by contacting the cells with an inducer compound that effects transcription from an inducible promoter operably linked to the FATP gene).
- The test agent (e.g., an agonist or antagonist) is added to the cells to be used in a
- 15 fatty acid transport assay, in the presence or absence of test agent, under conditions suitable for production and/or maintenance of the expressed FATP in a conformation appropriate for association of the FATP with test agent and substrate. For example, conditions under which an agent is assessed, such as media and temperature requirements, can, initially, be similar to those necessary for transport of typical fatty
- 20 acid substrates across the plasma membrane. One of ordinary skill in the art will know how to vary experimental conditions depending upon the biochemical nature of the test agent. The test agent can be added to the cells in the presence of fatty acid, or in the absence of fatty acid substrate, with the fatty acid substrate being added following the addition of the test agent. The concentration at which the test agent can be evaluated
- 25 can be varied, as appropriate, to test for an increased effect with increasing concentrations.

Test agents to be assessed for their effects on fatty acid transport can be any chemical (element, molecule, compound), made synthetically, made by recombinant

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techniques or isolated from a natural source. For example, test agents can be peptides, polypeptides, peptoids, sugars, hormones, or nucleic acid molecules, such as antisense nucleic acid molecules. In addition, test agents can be small molecules or molecules of greater complexity made by combinatorial chemistry, for example, and compiled into
5 libraries. These libraries can comprise, for example, alcohols, alkyl halides, amines, amides, esters, aldehydes, ethers and other classes of organic compounds. Test agents can also be natural or genetically engineered products isolated from lysates of cells, bacterial, animal or plant, or can be the cell lysates themselves. Presentation of test compounds to the test system can be in either an isolated form or as mixtures of
10 compounds, especially in initial screening steps.

Thus, the invention relates to a method for identifying agents which alter fatty acid transport, the method comprising providing the test agent to the cell (wherein "cell" includes the plural, and can include cells of a cell strain, cell line or culture of primary cells or organ culture, for example), under conditions suitable for binding to its target,
15 whether to the FATP itself or to another target on or in the cell, wherein the transformed cell comprises a FATP.

In greater detail, to test one or more agents or compounds (e.g., a mixture of compounds can conveniently be screened initially) for inhibition of the transport function of a fatty acid transport protein, the agent(s) can be contacted with the cells.
20 The cells can be contacted with a labeled fatty acid. The fatty acid can be, for example, a known substrate of the fatty acid transport protein such as oleate or palmitate. The fatty acid can itself be labeled with a radioactive isotope, (e.g., ^3H or ^{14}C) or can have a radioactively labeled adduct attached. In other variations, the fatty acid can have chemically attached to it a fluorescent label, or a substrate for an enzyme occurring
25 within the cells, wherein the substrate yields a detectable product, such as a highly colored or fluorescent product. Addition of candidate inhibitors and labeled substrate to the cells comprising fatty acid transport protein can be in either order or can be simultaneous.

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A second aliquot of cells, which can be called "control" cells (a "first" aliquot of cells can be called "test" cells), is treated, if necessary (as in the case of transformed "host" cells), so as to allow expression of the FATP gene, and is contacted with the labeled substrate of the fatty acid transport protein. The second aliquot of cells is not
5 contacted with one or more agents to be tested for inhibition of the transport function of the protein produced in the cells, but is otherwise kept under the same culture conditions as the first aliquot of cells.

In a further step of a method to identify inhibitors of a fatty acid transport protein, the labeled fatty acid is measured in the first and second aliquots of cells. A
10 preliminary step of this measurement process can be to separate the external medium from the cells so as to be able to distinguish the labeled fatty acid external to the cells from that which has been transported inside the cells. This can be accomplished, for instance, by removing the cells from their growth container, centrifuging the cell suspension, removing the supernatant and performing one or more wash steps to
15 extensively dilute the remaining medium which may contain labeled fatty acid. Detection of the labeled fatty acid can be by a means appropriate to the label used. For example, for a radioactive label, detection can be by scintillation counting of appropriately prepared samples of cells (e.g., lysates or protein extracts); for a fluorescent label, by measuring fluorescence in the cells by appropriate instrumentation.

20 If a compound tested as a candidate inhibitor of transport function causes the test cells to have less labeled fatty acid detected in the cells than that detected in the control cells, then the compound is an inhibitor of the fatty acid transport protein. Procedures analogous to those above can be devised for identifying enhancers (agonists of FATPs) of fatty acid transport function wherein if the test cells contain more labeled fatty acid
25 than that detected in the control cells, or if the fatty acid is taken up at a higher rate, then the compound being tested can be concluded to be an enhancer of the fatty acid transport protein.

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Example 13 describes use of an assay of this type to identify an inhibitor of a FATP. In Example 13, an antisense oligonucleotide which specifically inhibits biosynthesis of mmFATP4 was demonstrated to inhibit fatty acid uptake into mouse enterocytes. Similarly, antisense oligonucleotides directed towards specifically
5 inhibiting the biosynthesis of FATP6 in heart cells, FATP5 in liver cells, FATP3 in lung cells, and FATP2 in colon cells, can be demonstrated as examples of "test agents" that inhibit fatty acid transport.

Another assay to determine whether an agent is an inhibitor (or enhancer) of fatty acid transport employs animals, one or more of which are administered the agent,
10 and one or more of which are maintained under similar conditions, but are not administered the agent. Both groups of animals are given fatty acids (e.g., orally, intravenously, by tube inserted into stomach or intestine), and the fatty acids taken up into a bodily fluid (e.g., serum) or into an organ or tissue of interest are measured from comparable samples taken from each group of animals. The fatty acids may carry a
15 label (e.g., radioactive) to facilitate detection and quantitation of fatty acids taken up into the fluid or tissue being sampled. This type of assay can be used alone or can be used in addition to *in vitro* assays of a candidate inhibitor or enhancer.

An agent determined to be an inhibitor (or enhancer) of FATP function, such as fatty acid binding and/or fatty acid uptake, can be administered to cells in culture, or *in*
20 *vivo*, to a mammal (e.g. human) to inhibit (or enhance) FATP function. Such an agent may be one that acts directly on the FATP (for example, by binding) or can act on an intermediate in a biosynthetic pathway to produce FATP, such as transcription of the FATP gene, processing of the mRNA, or translation of the mRNA. An example of such an agent is antisense oligonucleotide.

25 Antisense methods similar to those illustrated in Example 13 can be used to determine the target FATP of a compound or agent that has an inhibitory or enhancing effect on fatty acid uptake. For example, antisense oligonucleotide directed to the inhibition of FATP4 biosynthesis can be added to lung cells or cell lines derived from

lung cells. In addition, antisense oligonucleotides directed to the inhibition of other FATPs, except for FATP3, can also be added to the lung cells. The administration of antisense oligonucleotides in this manner ensures that the predominant FATP activity remaining in the cells comes from FATP3. After a period of incubation of the cells with the antisense oligonucleotides sufficient to deplete the plasma membrane of the FATPs whose biosynthesis has been inhibited, a test agent, preferably one that has been shown by some preliminary test to have an inhibitory or enhancing activity on fatty acid transport, can be added to the lung cells. If the test agent is now demonstrated, after treatment of the cells with antisense oligonucleotides, to have an inhibitory or enhancing activity on fatty acid transport in the lung cells, it can be concluded that the target of the test agent is FATP3, or a molecule involved in the biosynthesis or activity of FATP3.

In another type of cell-based assay for uptake of fatty acids, a change of intracellular pH resulting from the uptake of fatty acids can be followed by an indicator fluorophore. The fluorophore can be taken up by the cells in a preincubation step. Fatty acids can be added to the cell medium, and after some period of incubation to allow FATP-mediated uptake of fatty acids, the change in λ_{\max} of fluorescence can be measured, as an indicator of a change in intracellular pH, as the λ_{\max} of fluorescence of the fluorophore changes with the pH of its environment, thereby indicating uptake of fatty acids. One such fluorophore is BCECF (2', 7'-bis(2-carboxyethyl)-5(6)-carboxyfluorescein; Rink, T.J. *et al.*, *J. Cell. Biol.* 95: 189 (1982)).

In assays similar to those described above, a candidate inhibitor or enhancer of fatty acid transport function can be added (or mock-added, for control cultures) to cultures of cells engineered to express a desired FATP to which fatty acid substrate is also added. Inhibition of fatty acid uptake is indicated by a lack of the drop in pH, indicating fatty acid uptake, that is seen in control cells. Enhancement of fatty acid uptake is indicated by a decrease in intracellular pH, as compared to control cells not receiving the candidate enhancer of fatty acid transport function.

Yeast cells can be used in a similar cell-based assay for the uptake of fatty acids mediated by a FATP, and such an assay can be adapted to a screening assay for the identification of agents that inhibit or enhance fatty acid uptake by an FATP. Yeast cells lacking an endogenous FATP activity (mutated, disrupted or deleted for *FAT1*;
5 Faergeman, N.J. *et al.*, *J. Biol. Chem.* 272(13):8531-8538 (1997); Watkins, P.A. *et al.*, *J. Biol. Chem.* 273(29):18210-18219 (1998)) can be engineered to harbor a related gene of the family of FATP-encoding genes, such as a mammalian FATP (e.g., human FATP4).

Examples of expression vectors include pEG (Mitchell, D.A., *et al.*, *Yeast* 9:715-
10 723 (1993)) and pDAD1 and pDAD2, which contain a *GAL1* promoter (Davis, L. I. and Fink, G. R., *Cell* 61:965-978 (1990)). A variety of promoters are suitable for expression. Available yeast vectors offer a choice of promoters. In one embodiment, the inducible *GAL1* promoter is used. In another embodiment, the constitutive *ADHI* promoter (alcohol dehydrogenase; Bennetzen, J. L. and Hall, B. D., *J. Biol. Chem.*
15 257:3026-3031 (1982)) can be used to express an inserted gene on glucose-containing media. An example of a vector suitable for expression of a heterologous FATP gene in yeast is pQB169.

With the introduced FATP gene providing the only fatty acid transport protein function for the yeast cells, it is possible to study effect of the heterologous FATP on
20 fatty acid transport into the yeast cells in isolation. Assays for the uptake of fatty acids into the yeast cells can be devised that are similar to those described above and/or those assays that have been illustrated in the Examples. Tests for candidate inhibitors or enhancers of the heterologous FATP can be done in cultures of yeast cells, wherein the yeast cells are incubated with fatty acid substrate and an agent to be tested as an
25 inhibitor or enhancer of FATP function. FATP uptake after a period of time can be measured by analyzing the contents of the yeast cells for fatty acid substrate, as compared with control yeast cells incubated with the fatty acid, but not with the test agent. Yeast cells have the additional advantage, over mammalian cells in culture, for

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example, that yeast cells can be forced to rely upon fatty acids as their only source of carbon, if the growth medium supplied to the yeast cells is formulated to contain no other source of carbon. Thus, the effect of the heterologous FATP on fatty acid uptake and metabolism in the engineered yeast cells can be amplified. An agent that efficiently
5 blocks transport function of the heterologous FATP could result in death of the yeast cells. Thus, in this case, inhibition of function of the heterologous FATP can result in loss of viability. A simple measure of viability is turbidity of the yeast suspension culture, which can be adapted to a high throughput screening assay for effects of various agents to be tested, using microtiter plates or similar devices for small-volume cultures
10 of the engineered yeast cells.

Cell-free assays can also be used to measure the transport of fatty acids across a membrane, and therefor also to assess a test treatment or test agent for its effect on the rate or extent of fatty acid transport. An isolated FATP, for example in the presence of a detergent that preserves the native 3-dimensional structure of the FATP, or partially
15 purified FATP, can be used in an artificial membrane system typically used to preserve the native conformation and activity of membrane proteins. Such systems include liposomes, artificial bilayers of phospholipids, isolated plasma membrane such as cell membrane fragments, cell membrane fractions, or cell membrane vesicles, and other systems in which the FATP can be properly oriented within the membrane to have
20 transport activity. Assays for transport activity can be performed using methods analogous to those that can be used in cells engineered to predominantly express one FATP whose function is to be measured. A labeled (e.g., radioactively labeled) fatty acid substrate can be incubated with one side of a bilayer or in a suspension of liposomes constructed to integrate a properly oriented FATP. The accumulation of fatty
25 acids with time can be measured, using appropriate means to detect the label (e.g., scintillation counting of medium on each side of the bilayer, or of the contents of liposomes isolated from the surrounding medium). Assays such as these can be adapted to use for the testing of agents which might interact with the FATP to produce an

inhibitory or an enhancing effect on the rate or extent of fatty acid transport. That is, the above-described assay can be done in the presence or absence of the agent to be tested, and the results compared.

For examples of isolation of membrane proteins (ADP/ATP carrier and
5 uncoupling protein), reconstitution into phospholipid vesicles, and assays of transport, see Klingenberg, M. *et al.*, *Methods Enzymol.* 260:369-389 (1995). For an example of a membrane protein (phosphate carrier of *Saccharomyces cerevisiae*) that was purified and solubilized from *E. coli* inclusion bodies, see Schroer, A. *et al.*, *J. Biol. Chem.* 273: 14269-14276 (1998). The Glut1 glucose transporter of rat has been expressed in yeast.
10 A crude membrane fraction of the yeast was prepared and reconstituted with soybean phospholipids into liposomes. Glucose transport activity could be measured in the liposomes (Kasahara, T. and Kasahara, M., *J. Biol. Chem.* 273: 29113-29117 (1998)). Similar methods can be applied to the proteins and polypeptides of the invention.

Another embodiment of the invention is a method for inhibiting fatty acid
15 uptake in a mammal (e.g., a human), comprising administering to the mammal a therapeutically effective amount of an inhibitor of the transport function of one or more of the fatty acid transport proteins, thereby decreasing fatty acid uptake by cells comprising the fatty acid protein(s). Where it is desirable to reduce the uptake of fatty acids, for example, in the treatment of chronic obesity or as a part of a program of
20 weight control or hyperlipidemia control in a human, one or more inhibitors of one or more of the fatty acid transport proteins can be administered in an effective dose, and by an effective route, for example, orally, or by an indwelling device that can deliver doses to the small intestine. The inhibitor can be one identified by methods described herein, or can be one that is, for instance, structurally related to an inhibitor identified by
25 methods described herein (e.g., having chemical adducts to better stabilize or solubilize the inhibitor). The invention further relates to compositions comprising inhibitors of fatty acid uptake in a mammal, which may further comprise pharmaceutical carriers

suitable for administration to a subject mammal, such as sterile solubilizing or emulsifying agents.

A further embodiment of the present invention is a method of enhancing or increasing fatty acid uptake, such as enhancing or increasing LCFA uptake in the small intestine (e.g., to treat or prevent a malabsorption syndrome or other wasting condition) or in the liver (e.g., by an enhancer of FATP5 transport activity to treat acute liver failure) or in the kidney (e.g., by an enhancer of FATP2 transport activity to treat kidney failure). In this embodiment, a therapeutically effective amount of an enhancer of the transport function of one or more of the fatty acid transport proteins can be administered to a mammalian subject, with the result that fatty acid uptake in the small intestine is enhanced. In this embodiment, one or more enhancers of one or more of fatty acid transport proteins is administered in an effective dose and by a route (e.g., orally or by a device, such as an indwelling catheter or other device) which can deliver doses to the gut. The enhancer of FATP function (e.g., an enhancer of FATP4 function) can be identified by methods described herein or can be one that is structurally similar to an enhancer identified by methods described herein.

Aerobic reperfusion of ischemic myocardium is a common clinical event which can occur during such treatments as cardiac surgery, angioplasty, and thrombolytic therapy after a myocardial infarction. During reperfusion, a rapid recovery of myocardial energy production is essential for the complete recovery of contractile function. Not only the extent of recovery of myocardial energy metabolism but also the type of energy substrate used by the heart during reperfusion are important determinants of functional recovery. Circulating fatty acid levels increase following acute myocardial infarction or during cardiac surgery, such that during and following ischemia the heart muscle can be exposed to very high concentrations of fatty acids (Lopaschuk, G.D. and W. C. Stanley, *Science and Medicine* (November/December 1997)). High plasma fatty acid concentrations increase the severity of ischemic damage in a number of experimental models of cardiac ischemia and have been linked to

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depression of mechanical function during aerobic reperfusion of previously ischemic hearts. Further data show that modifying fatty acid utilization can be beneficial for heart function in ischemia and can be a useful approach for the treatment of angina. See, e.g., Desideri and Celegon, *Am. J. Cardiol.* 82(5A):50K-53K; Lopaschuk, *Am. J. Cardiol.* 82(5A):14K-17K. Plasma fatty acid concentrations can be reduced by administering to a human subject or other mammal an effective amount of an inhibitor of a FATP such as FATP2 or FATP4, thereby providing a way of reducing fatty acid utilization by the heart.

In a further embodiment of the invention, a therapeutically effective amount of an inhibitor of hsFATP6 can be administered to a human patient by a suitable route, to reduce the uptake of fatty acids by cardiac muscle. This treatment is desirable in patients who are diagnosed as having, or who are at risk of, abnormal accumulations of fatty acids in the heart or a detrimentally high rate of uptake of fatty acids into the heart, because of ischemic heart disease, or following ischemia or trauma to the heart.

The invention further relates to antibodies that bind to an isolated or recombinant fatty acid transport protein of the FATP family, including portions of antibodies, which can specifically recognize and bind to one or more FATPs. The antibodies and portions thereof of the invention include those which bind to one or more FATPs of mouse or other mammalian species. In a preferred embodiment, the antibodies specifically bind to a naturally occurring FATP of humans. The antibodies can be used in methods to detect or to purify a protein of the present invention or a portion thereof by various methods of immunoaffinity chromatography, to inhibit the function of a protein in a method of therapy, or to selectively inactivate an active site, or to study other aspects of the structure of these proteins, for example.

The antibodies of the present invention can be polyclonal or monoclonal. The term antibody is intended to encompass both polyclonal and monoclonal antibodies. Antibodies of the present invention can be raised against an appropriate immunogen, including proteins or polypeptides of the present invention, such as an isolated or

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recombinant FATP1, FATP2, FATP3, FATP4, FATP5, FATP6, mtFATP, ceFATPa, ceFATPb, scFATP or portions thereof, or synthetic molecules, such as synthetic peptides (e.g., conjugated to a suitable carrier). Preferred embodiments are antibodies that bind to any of the following: hsFATP1, hsFATP2, hsFATP3, hsFATP4, hsFATP5
5 or hsFATP6. The immunogen can be a polypeptide comprising a portion of a FATP and having at least one function of a fatty acid transport protein, as described herein.

The term antibody is also intended to encompass single chain antibodies, chimeric, humanized or primatized (CDR-grafted) antibodies and the like, as well as chimeric or CDR-grafted single chain antibodies, comprising portions from more than
10 one species. For example, the chimeric antibodies can comprise portions of proteins derived from two different species, joined together chemically by conventional techniques or prepared as a single contiguous protein using genetic engineering techniques (e.g., DNA encoding the protein portions of the chimeric antibody can be expressed to produce a contiguous protein chain. See, e.g., Cabilly *et al.*, U.S. Patent
15 No. 4,816,567; Cabilly *et al.*, European Patent No. 0,125,023 B1; Boss *et al.*, U.S. Patent No. 4,816,397; Boss *et al.*, European Patent No. 0,120,694 B1; Neuberger, M.S. *et al.*, WO 86/01533; Neuberger, M.S. *et al.*, European Patent No. 0,194,276 B1; Winter, U.S. Patent No. 5,225,539; Winter, European Patent No. 0,239,400 B1; Queen *et al.*, U.S. Patent No. 5,585,089; and Queen *et al.*, European Patent No. EP 0 451 216
20 B1. See also, Newman, R. *et al.*, *BioTechnology*, 10:1455-1460 (1992), regarding primatized antibody, and Ladner *et al.*, U.S. Patent No. 4,946,778 and Bird, R.E. *et al.*, *Science*, 242:423-426 (1988) regarding single chain antibodies.)

Whole antibodies and biologically functional fragments thereof are also encompassed by the term antibody. Biologically functional antibody fragments which
25 can be used include those fragments sufficient for binding of the antibody fragment to a FATP to occur, such as Fv, Fab, Fab' and F(ab')₂ fragments. Such fragments can be produced by enzymatic cleavage or by recombinant techniques. For instance, papain or pepsin cleavage can generate Fab or F(ab')₂ fragments, respectively. Antibodies can

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also be produced in a variety of truncated forms using antibody genes in which one or more stop codons have been introduced upstream of the natural stop site. For example, a chimeric gene encoding a F(ab')₂ heavy chain portion can be designed to include DNA sequences encoding the CH₁ domain and hinge region of the heavy chain.

- 5 Preparation of immunizing antigen (whole cells comprising FATP on the cell surface or purified FATP), and polyclonal and monoclonal antibody production can be performed using any suitable technique. A variety of methods have been described (See e.g., Kohler *et al.*, *Nature*, 256: 495-497 (1975) and *Eur. J. Immunol.* 6: 511-519 (1976); Milstein *et al.*, *Nature* 266: 550-552 (1977); Koprowski *et al.*, U.S. Patent No. 4,172,124; Harlow, E. and D. Lane, 1988, *Antibodies: A Laboratory Manual*, (Cold Spring Harbor Laboratory: Cold Spring Harbor, NY); Chapter 11 In *Current Protocols In Molecular Biology*, Vol. 2 (containing supplements up through Supplement 42, 1998), Ausubel, F.M. *et al.*, eds., (John Wiley & Sons: New York, NY)). Generally, a hybridoma can be produced by fusing a suitable immortal cell line (e.g., a myeloma cell
- 10 line such as SP2/0) with antibody producing cells. The antibody producing cells, preferably those obtained from the spleen or lymph nodes, can be obtained from animals immunized with the antigen of interest. Immunization of animals can be by introduction of whole cells comprising fatty acid transport protein on the cell surface. The fused cells (hybridomas) can be isolated using selective culture conditions, and
- 15 cloned by limiting dilution. Cells which produce antibodies with the desired specificity can be selected by a suitable assay (e.g., ELISA).

- Other suitable methods of producing or isolating antibodies (including human antibodies) of the requisite specificity can be used, including, for example, methods which select recombinant antibody from a library (e.g., Hoogenboom *et al.*, WO 93/06213; 25 Hoogenboom *et al.*, U.S. Patent No. 5,565,332; WO 94/13804, published June 23, 1994; and Dower, W.J. *et al.*, U.S. Patent No. 5,427,908), or which rely upon immunization of transgenic animals (e.g., mice) capable of producing a full repertoire of human antibodies (see e.g., Jakobovits *et al.*, *Proc. Natl. Acad. Sci. USA*, 90: 2551-2555

(1993); Jakobovits *et al.*, *Nature*, 362:255-258 (1993); Lonberg *et al.*, U.S. Patent No. 5,569,825; Lonberg *et al.*, U.S. Patent No. 5,545,806; Surani *et al.*, U.S. Patent No. 5,545,807; and Kucherlapati, R. *et al.*, European Patent No. EP 0 463 151 B1).

Another aspect of the invention is a method for directing an agent to cardiac muscle. The differential expression of FATP6 in cardiac muscle but not in other tissue types allows for the specific targeting of drugs, diagnostic agents, tagging labels, histological stains or other substances specifically to cardiac muscle. A targeting vehicle can be used for the delivery of such a substance. Targeting vehicles which bind specifically to FATP6 can be linked to a substance to be delivered to the cells of cardiac muscle. The linkage can be, for instance, via one or more covalent bonds, or by high affinity non-covalent bonds. A targeting vehicle can be an antibody, for instance, or other compound (e.g., a fatty acid or fatty acid analog) which binds to FATP6 with high specificity.

Targeting vehicles specific to the heart-specific protein FATP6 have *in vivo* (e.g., therapeutic and diagnostic) applications. For example, an antibody which specifically binds to FATP6 can be conjugated to a drug to be targeted to the heart (e.g., a cardiac glycoside to treat congestive heart failure, or β -adrenergic agents, sodium channel blockers or calcium channel blockers to treat arrhythmias). A substance (e.g., a radioactive substance) which can be detected (e.g., a label) *in vivo* can also be linked to a targeting vehicle which specifically binds to a heart-specific protein such as FATP6, and the conjugate can be used as a labeling agent to identify cardiac muscle cells.

Targeting vehicles specific to FATP6 find further applications *in vitro*. For example, an FATP6-specific targeting vehicle, such as an antibody (a polyclonal preparation or monoclonal) which specifically binds to FATP6, can be linked to a substance which can be used as a stain for a tissue sample (e.g., horseradish peroxidase) to provide a method for the identification of cardiac muscle in a sample, as can be used in embryology studies, for example.

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In a similar manner, an agent can be directed to the liver of a mammal, as FATP5 is expressed in liver but not in other tissue types. A targeting vehicle which specifically binds to FATP5 can be conjugated to a drug for delivery of the drug to the liver, such as a drug to treat hepatitis, Wilson's disease, lipid storage diseases and liver cancer. As with targeting vehicles specific to FATP6, targeting vehicles specific to FATP5 can be used in studying tissue samples *in vitro*.

The invention also relates to compositions comprising a modulator of FATP function. The term "modulate" as used herein refers to the ability of a molecule to alter the function of another molecule. Thus, modulate could mean, for example, inhibit, antagonize, agonize, upregulate, downregulate, induce, or suppress. A modulator has the capability of altering function of its target. Such alteration can be accomplished at any stage of the transcription, translation, expression or function of the protein, so that, for example, modulation of a target gene can be accomplished by modulation of the DNA or RNA encoding the protein, and the protein itself.

Antagonists or agonists (inhibitors or enhancers) of the FATPs of the invention, antibodies that bind a FATP, or mimetics of a FATP can be employed in combination with a non-sterile or sterile carrier or carriers for use with cells, tissues or organisms, such as a pharmaceutical carrier suitable for administration to a mammalian subject. Such compositions comprise, for instance, a media additive or a therapeutically effective amount of an inhibitor or enhancer compound to be identified by an assay of the invention and a pharmaceutically acceptable carrier or excipient. Such carriers may include, but are not limited to, saline, buffered saline, dextrose, water, ethanol, surfactants, such as glycerol, excipients such as lactose and combinations thereof. The formulation can be chosen by one of ordinary skill in the art to suit the mode of administration. The chosen route of administration will be influenced by the predominant tissue or organ location of the FATP whose function is to be inhibited or enhanced. For example, for affecting the function of FATP4, a preferred administration can be oral or through a tube inserted into the stomach (e.g., direct stomach tube or

nasopharyngeal tube), or through other means to accomplish delivery to the small intestine. The invention further relates to diagnostic and pharmaceutical packs and kits comprising one or more containers filled with one or more of the ingredients of the aforementioned compositions of the invention.

5 Compounds of the invention which are FATPs, FATP fusion proteins, FATP mimetics, FATP gene-specific antisense poly- or oligonucleotides, inhibitors or enhancers of a FATP may be employed alone or in conjunction with other compounds, such as therapeutic compounds. The pharmaceutical compositions may be administered in any effective, convenient manner, including administration by topical, oral, anal,
10 vaginal, intravenous, intraperitoneal, intramuscular, subcutaneous, intranasal, transdermal or intradermal routes, among others. In therapy or as a prophylactic, the active agent may be administered to an individual as an injectable composition, for example as a sterile aqueous dispersion, preferably isotonic.

 Alternatively, the composition may be formulated for topical application, for
15 example, in the form of ointments, creams, lotions, eye ointments, eye drops, ear drops, mouthwash, impregnated dressings and sutures and aerosols, and may contain appropriate conventional additives, including, for example, preservatives, solvents to assist drug penetration, and emollients in ointments and creams. Such topical formulations may also contain compatible conventional carriers, for example cream or
20 ointment bases, and ethanol or oleyl alcohol for lotions.

 In addition, the amount of the compound will vary depending on the size, age, body weight, general health, sex, and diet of the host, and the time of administration, the biological half-life of the compound, and the particular characteristics and symptoms of the disorder to be treated. Adjustment and manipulation of established dose ranges are
25 well within the ability of those of skill in the art.

 A further aspect of the invention is a method to identify a polymorphism, or the presence of an alternative or variant allele of a gene in the genome of an organism (of interest here, genes encoding FATPs). As used herein, polymorphism refers to the

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occurrence of two or more genetically determined alternative sequences or alleles in a population. A polymorphic locus may be as small as a base pair. Polymorphic markers include restriction fragment length polymorphisms, variable number of tandem repeats (VNTR's), hypervariable regions, minisatellites, dinucleotide repeats, trinucleotide repeats, tetranucleotide repeats, simple sequence repeats, and insertion elements such as Alu. The first identified allelic form, or the most frequently occurring form can be arbitrarily designated as the reference (usually, "wildtype") form, and other allelic forms are designated as alternative (sometimes, "mutant" or "variant"). Diploid organisms may be homozygous or heterozygous for allelic forms.

10 An "allele" or "allelic sequence" is an alternative form of a gene which may result from at least one mutation in the nucleotide sequence. Alleles may result in altered mRNAs or polypeptides whose structure or function may or may not be altered. Any given gene may have none, one, or many allelic forms (polymorphism). Common mutational changes which give rise to alleles are generally ascribed to natural deletions, additions, or substitutions of nucleotides. Each of these types of changes may occur alone, or in combination with the others, one or more times in a given sequence.

Several different types of polymorphisms have been reported. A restriction fragment length polymorphism (RFLP) is a variation in DNA sequence that alters the length of a restriction fragment (Botstein *et al.*, *Am. J. Hum. Genet.* 32:314-331 (1980)).

20 The restriction fragment length polymorphism may create or delete a restriction site, thus changing the length of the restriction fragment. RFLPs have been widely used in human and animal genetic analyses (see WO 90/13668; WO 90/11369; Donis-Keller, *Cell* 51:319-337 (1987); Lander *et al.*, *Genetics* 121:85-99 (1989)). When a heritable trait can be linked to a particular RFLP, the presence of the RFLP in an individual can

25 be used to predict the likelihood that the individual will also exhibit the trait.

Other polymorphisms take the form of short tandem repeats (STRs) that include tandem di-, tri- and tetra-nucleotide repeated motifs. These tandem repeats are also referred to as variable number tandem repeat (VNTR) polymorphisms. VNTRs have

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been used in identity and paternity analysis (US 5,075,217; Armour *et al.*, *FEBS Lett.* 307:113-115 (1992); Horn *et al.*, WO 91/14003; Jeffreys, EP 370,719), and in a large number of genetic mapping studies.

Other polymorphisms take the form of single nucleotide variations between individuals of the same species. Such polymorphisms are far more frequent than RFLPs, STRs (short tandem repeats) and VNTRs (variable number tandem repeats). Some single nucleotide polymorphisms occur in protein-coding sequences, in which case, one of the polymorphic forms may give rise to the expression of a defective or other variant protein and, potentially, a genetic disease. Other single nucleotide polymorphisms occur in noncoding regions. Some of these polymorphisms may also result in defective protein expression (e.g., as a result of defective splicing). Other single nucleotide polymorphisms have no phenotypic effects.

Many of the methods described below require amplification of DNA from target samples and purification of the amplified products. This can be accomplished by PCR, for instance. See generally, *PCR Technology, Principles and Applications for DNA Amplification* (ed. H.A. Erlich), Freeman Press, New York, NY, 1992; *PCR Protocols: A Guide to Methods and Applications* (eds. Innis, et al.), Academic Press, San Diego, CA, 1990; Mattila *et al.*, *Nucleic Acids Res.* 19:4967 (1991); Eckert *et al.*, *PCR Methods and Applications* 1:17 (1991); *PCR* (eds. McPherson *et al.*, IRS Press, Oxford); and US 4,683,202.

Other suitable amplification methods include the ligase chain reaction (LCR) (see Wu and Wallace, *Genomics* 4:560 (1989); Landegren *et al.*, *Science* 241:1077 (1988)), transcription amplification (Kwoh *et al.*, *Proc. Natl. Acad. Sci. USA* 86:1173 (1989); self-sustained sequence replication (Guatelli *et al.*, *Proc. Natl. Acad. Sci. USA* 87:1874 (1990)), and nucleic acid based sequence amplification (NASBA). The latter two amplification methods involve isothermal reactions based on isothermal transcription, which produce both single stranded RNA (ssRNA) and double stranded

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DNA (dsDNA) as the amplification products in a ratio of about 30 or 100 to 1, respectively.

Another aspect of the invention is a method for detecting a variant allele of a human FATP gene, comprising preparing amplified, purified FATP DNA from a reference human and amplified, purified, FATP DNA from a "test" human to be compared to the reference as having a variant allele, using the same or comparable amplification procedures, and determining whether the reference DNA and test DNA differ in DNA sequence in the FATP gene, whether in a coding or a noncoding region, wherein, if the test DNA differs in sequence from the reference DNA, the test DNA comprises a variant allele of a human FATP gene. The following is a discussion of some of the methods by which it can be determined whether the reference FATP DNA and test FATP DNA differ in sequence.

Direct Sequencing. The direct analysis of the sequence of variant alleles of the present invention can be accomplished using either the dideoxy chain termination method or the Maxam and Gilbert method (see Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Press, New York 1989; Zyskind *et al.*, *Recombinant DNA Laboratory Manual*, Acad. Press, 1988)).

Denaturing Gradient Gel Electrophoresis. Amplification products generated using the polymerase chain reaction can be analyzed by the use of denaturing gradient gel electrophoresis. Different alleles can be identified based on the different sequence-dependent strand dissociation properties and electrophoretic migration of DNA in solution (chapter 7 in Erlich, ed. *PCR Technology, Principles and Applications for DNA Amplification*, W.H. Freeman and Co., New York, 1992).

Single-strand Conformation Polymorphism Analysis. Alleles of target sequences can be differentiated using single-strand conformation polymorphism analysis, which identifies base differences by alteration in electrophoretic migration of single stranded PCR products, as described in Orita *et al.*, *Proc. Natl. Acad. Sci. USA* 86:2766-2770 (1989). Amplified PCR products can be generated as described above,

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and heated or otherwise denatured, to form single-stranded amplification products. Single-stranded nucleic acids may refold or form secondary structures which are partially dependent on the base sequence. The different electrophoretic mobilities of single-stranded amplification products can be related to base-sequence differences
5 between alleles of target sequences.

Detection of Binding by Protein That Binds to Mismatches. Amplified DNA comprising the FATP gene or portion of the gene of interest from genomic DNA, for example, of a normal individual is prepared, using primers designed on the basis of the DNA sequences provided herein. Amplified DNA is also prepared, in a similar manner,
10 from genomic DNA of an individual to be tested for bearing a distinguishable allele. The primers used in PCR carry different labels, for example, primer 1 with biotin, and primer 2 with ³²P. Unused primers are separated from the PCR products, and the products are quantitated. The heteroduplexes are used in a mismatch detection assay using immobilized mismatch binding protein (MutS) bound to nitrocellulose. The
15 presence of biotin-labeled DNA wherein mismatched regions are bound to the nitrocellulose via MutS protein, is detected by visualizing the binding of streptavidin to biotin. See WO 95/12689. MutS protein has also been used in the detection of point mutations in a gel-mobility-shift assay (Lishanski, A. *et al.*, *Proc. Natl. Acad. Sci. USA* 91:2674-2678 (1994)).

20 Other methods, such as those described below, can be used to distinguish a FATP allele from a reference allele, once a particular allele has been characterized as to DNA sequence.

Allele-specific probes. The design and use of allele-specific probes for analyzing polymorphisms is described by e.g., Saiki *et al.*, *Nature* 324:163-166 (1986);
25 Dattagupta, EP 235,726, Saiki, WO 89/11548. Allele-specific probes can be designed so that they hybridize to a segment of a target DNA from one individual but do not hybridize to the corresponding segment from another individual due to the presence of different polymorphic forms in the respective segments from the two individuals.

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Hybridization conditions should be sufficiently stringent that there is a significant difference in hybridization intensity between alleles, and preferably an essentially binary response, whereby a probe hybridizes to only one of the alleles. Some probes are designed to hybridize to a segment of target DNA such that the polymorphic site aligns with a central position (e.g., in a 15-mer at the 7 position; in a 16-mer, at either the 8 or 9 position) of the probe. This design of probe achieves good discrimination in hybridization between different allelic forms.

Allele-specific probes are often used in pairs, one member of a pair showing a perfect match to a reference form of a target sequence and the other member showing a perfect match to a variant form. Several pairs of probes can then be immobilized on the same support for simultaneous analysis of multiple polymorphisms within the same target sequence.

Allele-specific Primers. An allele-specific primer hybridizes to a site on target DNA overlapping a polymorphism, and only primes amplification of an allelic form to which the primer exhibits perfect complementarity. See Gibbs, *Nucleic Acid Res.* 17:2427-2448 (1989). This primer is used in conjunction with a second primer which hybridizes at a distal site. Amplification proceeds from the two primers, resulting in a detectable product which indicates the particular allelic form is present. A control is usually performed with a second pair of primers, one of which shows a single base mismatch at the polymorphic site and the other of which exhibits perfect complementarity to a distal site. The single-base mismatch prevents amplification and no detectable product is formed. The method works best when the mismatch is included in the 3'-most position of the oligonucleotide aligned with the polymorphism because this position is most destabilizing to elongation from the primer (see, e.g., WO 93/22456).

Gene Chips. Allelic variants can also be identified by hybridization to nucleic acids immobilized on solid supports (gene chips), as described, for example, in WO 95/11995 and U.S. Patent No. 5,143,854, both of which are incorporated herein by

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reference. WO 95/11995 describes subarrays that are optimized for detection of a characterized variant allele. Such a subarray contains probes designed to be complementary to a second reference sequence, which is an allelic variant of the first reference sequence.

- 5 The present method is illustrated by the following examples, which are not intended to be limiting in any way.

EXAMPLES

Materials and Methods

The following Materials and Methods were used in the work described in

10 Examples 1-5.

Sequence Alignment of FATP Clones. The DNA sequence for mouse FATP1 was obtained from the National Center for Biotechnology Information nonredundant database. cDNAs for mmFATP2, 3, 4, and 5 were obtained by screening mouse expression libraries (purchased from GIBCO/BRL) with probes derived from the cloned
15 expressed sequence tags (ESTs) (Research Genetics, Huntsville, AL). Full-length clones were obtained for mmFATP2 and 5 and partial sequences for mmFATP3 and 4. The sequences described herein have been deposited in the GenBank database (Accession Nos. FATP2, AF072760; FATP3, AF072759; FATP4, AF072758; FATP5, AF072757).

- 20 Neither FATP2 nor FATP5 contains an in-frame stop codon upstream of the putative initiator methionine; initiator methionines were assigned by homology with that in mmFATP1 and by the presence of a signal sequence immediately after it. The *Mycobacterium tuberculosis*, *Caenorhabditis elegans*, and *Saccharomyces cerevisiae* sequences were present in the dbEST database as part of the sequencing projects for
25 these organisms. Sequences were aligned utilizing a ClustalX algorithm and the resulting alignment exported to SeqVu. Homologous amino acid substitutions are

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boxed in Figure 1 and were determined using the Dayhoff 250 method with a 50% homology cutoff.

Cell Transfection and LCFA Uptake. COS cells were cotransfected using the DEAE-dextran method with the mammalian expression vector pCDNA 3.1 (Invitrogen) expressing the gene for CD2 (pCDNA-CD2) in combination with either a pCDNA 3.1 or pCMVSPORT2 (GIBCO/BRL) expression vector containing one of the murine or nematode *FATP* genes (*pCDNA-mmFATP1*, *pCDNA-FATP2*, *pCMVSPORT-FATP5*, *pCDNA-ceFATPb*). Two days after transfection, cells were assayed for CD2 expression with a phycoerythrin-coupled anti-CD2(PE-CD2) monoclonal antibody (PharMingen), and fatty acid uptake was assayed with a BODIPY-labeled fatty acid analogue (Molecular Probes). Briefly, cells were washed twice with PBS (phosphate buffered saline) and stained with PE-CD2 at 4°C for 30 min in PBS containing 10% fetal calf serum. They were then washed three times with PBS/fetal calf serum for 5 min followed by an incubation for 2 min at 37°C in fatty acid uptake solution, which contained 0.1 µM BODIPY-FA and 0.1% fatty acid-free BSA (bovine serum albumin) in PBS (Schaffer, J.E. & Lodish, H.F. (1994) *Cell* 79:427-436). After 2 min, the cells were washed four times with ice-cold PBS/0.1% BSA. The cells were then removed from the plates with PBS containing 5 mM EDTA and resuspended in PBS containing 10% fetal calf serum and 10 mM EDTA. PE-CD2 and BODIPY-FA fluorescence were measured using a FACScan (Becton Dickinson). COS cells were gated on forward scatter (FSC) and side scatter (SS). Cells exhibiting more than 300 CD2 fluorescence units (dsim) representing 15% of all cells were deemed CD2 positive and their BODIPY-FA fluorescence was quantitated.

E. coli-Based LCFA Uptake Assay. The full-length coding region of mtFATP and a control protein, the mammalian transcription factor TFE3, were subcloned into the inducible, prokaryotic expression vector pET (Novagen). Expression was induced with 1 mM isopropyl β-D-thiogalactoside (IPTG) for 1 hour, or cells were left uninduced. Cells were washed in PBS/0.1% BSA and resuspended in 1 ml PBS/0.1% BSA

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containing 0.1 μ M [3 H]palmitate (NEN) at 37°C. Uptake was stopped after the indicated incubation time by transferring the cells onto filter paper using a cell harvester (Brandel, Bethesda, MD). Filters were washed extensively with ice-cold PBS/0.1% BSA, and [3 H]palmitate was quantitated by scintillation counting.

5 Northern Blots. Northern blot analysis of murine FATP expression was done using poly(A) mRNA blots (Clontech). Probes of each of the FATPs were derived from the 3' untranslated regions of each gene and were <60% identical in sequence. Probes were labeled by random priming (Boehringer Mannheim) and hybridized at 65°C. Blots were extensively washed in 0.2% SSC/0.1% SDS at 65°C.

10 Generation of Phylogenetic Trees. Complete and partial sequences for *FATP* genes from human, rat, mouse, puffer fish, *Drosophila melanogaster*, *C. elegans*, *S. cerevisiae*, and *M. tuberculosis* were aligned using ClustalX. A homologous region of 48 amino acids (residues 472-519 in mmFATP1) from all of the genes was used to determine phylogenetic relationship within ClustalX. Based on these data a
15 phylogenetic tree was generated using Tree View PPC (Figure 5).

Nomenclature. It is proposed that the *FATP* genes be given a species specific prefix (mm, *Mus musculus*; hs, *Homo sapiens*; mt, *M. tuberculosis*; dm, *D. melanogaster*; ce, *C. elegans*, sc, *S. cerevisiae*) and numbered such that mammalian homologues in different species share the same number but differ in their prefix. Since
20 the two *C. elegans* genes cannot be paired with a specific human or mouse FATP, they have been designated *ceFATPa* and *ceFATPb*.

Example 1: Identification of Novel Mammalian FATPs

The National Center for Biotechnology Information EST database was screened, using the mouse FATP protein sequence (mmFATP1), to identify novel FATPs. This
25 strategy led to the identification of more than 50 murine EST sequences which could be assembled into five distinct contiguous DNA sequences (contigs). One contig was identical to the previously cloned FATP, which has been renamed FATP1. Another,

which has been renamed FATP2, is the murine homologue of a rat gene previously identified by others as a very long chain acyl-CoA synthase (Uchiyama, A., Aoyama, T., Kamijo, K., Uchida, Y., Kondo, N., Orii, T. & Hashimoto, T. (1996) *J. Biol. Chem.* 271:30360-30365). The other three contigs represented novel genes (*FATP3*, 4, and 5).

- 5 Full-length clones for *FATP2* and *FATP5* and nearly complete sequences for *FATP3* and 4 (Figure 1) were obtained by screening cDNA libraries made from mouse day 10.5 embryos and adult liver. Also identified were human homologues for each of the murine genes in the EST database. A sixth human gene was also identified; whether this gene is also present in the mouse will require additional studies. Map positions are
10 given in Tables 2 and 3.

The genetic loci for all of the human genes, with the exception of *FATP5* which was already mapped as an unknown EST, were determined using the radiation hybrid panels. The map positions given below show the distance (in centiRays) from the closest framework marker. As a guideline, there are approximately 300kb/cR.

Table 2. Mapping Data for Human Genes

	hsFATP1	Chromosome Chr19 places 13.35 cR from WI-6344 (lod>3.0)
	hsFATP2	Chromosome Chr15 places 4.92 cR from D15S126 (lod>3.0)
5		
	hsFATP3	Chromosome Chr1 places 13.24 cR from WI-2862 (lod>3.0)
	hsFATP4	Chromosome Chr9 places 7.80 cR from WI-9685 (lod>3.0)
10	hsFATP5	unknown EST previously mapped to near D19S418
	hsFATP6	Chromosome Chr5 places 1.41 cR from WI-4907 (lod>3.0)

The mouse map is an internal backcross panel consisting of 188 mouse backcross DNA's plus 4 controls (B6, Spretus, F1, Water). The backcross was constructed by crossing B6 by Spretus animals and then crossing those F1's back to B6. Mapping is accomplished by taking advantage of recombinational events during meiosis, and the use of PCR primers to detect the differences (by size or re-annealing events) at any given locus between the B6 and Spretus allele.

For the purposes of mapping, a novel set of primers (gene of interest) is used to amplify from all 188 DNA's and then typed as being a B6 ("B") or a Spretus ("S"). This string of B's and S's is entered into the Map Manager program, which does a best fit calculation by comparing the string of 188 typings from the gene of interest to all loci already extant in the panel, for all 20 chromosomes. The gene of interest is then assigned to a particular area on a particular chromosome according to a number of parameters, including the minimalization of double cross-overs, and the highest LOD

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scores. Indicated in Table 3 are distances to the closest markers on either side of the FATP locus.

Table 3. Mapping Data for Mouse Genes

5	nmFATP1	Chromosome 8
		places 2.82 cM from D8Mit132 (lod 43.4) and 1.81 cM from D8Mit74 (lod 43.5)
10	mmFATP2	Chromosome 2
		places 1.29 cM from D2Mit258 (lod 47.9) and 1.75 cM from D2NDS3 (lod 44.9)
15	mmFATP3	Chromosome 3
		places 2.54 cM from D3Mit22 (lod 29.5) and 19.62 cM from D3Mit42 (lod 13.6)
20	mmFATP4	Chromosome 2
		places 13.78 cM from D2Mit1 (lod 22.9) and 3.85 cM from D2Mit65 (lod 41.9)
25	mmFATP5	Chromosome 7
		places 7.28 cM proximal of D7Mit21 (lod 28.3)

Example 2: Assessment of Function

The ability of the newly identified mouse genes to function as fatty acid transporters was assessed using a fluorescence-activated cell sorting-based assay. COS cells were transiently cotransfected with expression vectors encoding the cell surface protein CD2 and either mmFATP1, mmFATP2, or mmFATP5, respectively. Two days after transfection, COS cells were stained with an antibody to CD2 and then incubated with a BODIPY-labeled fatty acid [BODIPY-FA, (Schaffer, J.E. & Lodish, H.F. (1994) *Cell* 79:427-436)]. The cells were then washed extensively, lifted off the dish, and

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analyzed by fluorescence-activated cell sorting. As judged by the number of CD2-positive cells, the transfection efficiency was approximately 20-30%. Fatty acid uptake was quantitated in the transiently transfected COS cells by measuring the BODIPY-FA fluorescence of the CD2-positive cells. Expression of CD2 had no effect on fatty acid uptake as shown by the finding that COS cells expressing only the transfected CD2 cDNA (CD2-positive) had the same low level of BODIPY-FA uptake as did untransfected (CD2-negative) control cells (Figure 2A, control). In COS cells cotransfected with CD2 and mmFATP1, mmFATP2, or mmFATP5, uptake of BODIPY-FA by the transfected (CD2-positive) cells was increased between 15- to 90- fold over control (CD2 cDNA only) cells (Figures 2A-2D).

Example 3: Expression Patterns of Murine FATPs

Expression patterns of members of the murine *FATP* gene family were characterized by Northern blot analysis; to avoid cross-hybridization, the probes used were from the 3' untranslated region of these genes, which are less than 60% identical in sequence. The expression pattern of FATP1 agrees with that previously found (Schaffer, J.E. & Lodish, H.F. (1994) *Cell* 79:427-436). Here, expression was seen primarily in heart and kidney. FATP2 is expressed almost exclusively in liver and kidney, which corresponds to the reported tissue distribution of the rat homologue [very long chain acyl-CoA (VLACS)] as assessed by Western blotting (Uchiyama, A., Aoyama, T., Kamijo, K., Uchida, Y., Kondo, N., Orii, T. & Hashimoto, T. (1996) *J. Biol. Chem.* 271:30360-30365). FATP3 is present in lung, liver, and testis. FATP5 is expressed only in liver and cannot be detected in other tissues even when the blot is overexposed. The human homologue of FATP5 is also liver specific and is not expressed in a wide array of other tissues tested, including fetal liver.

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Example 4: FATPs Are Evolutionarily Conserved

The EST database was searched, using sequences conserved among the five murine FATP genes, for *FATP* genes in other organisms. Two homologues were found in *C. elegans* and one in *M. tuberculosis*. One of the *C. elegans* genes was cloned from a cDNA library and expressed in COS cells, as described for the murine FATPs. Overexpression of the nematode FATP resulted in a 15-fold increase of BODIPY-FA uptake compared with control cells (Figure 3). The mycobacterial *FATP* gene was isolated from a phage library and assessed for its ability to facilitate fatty acid uptake. *E. coli* transformed with a prokaryotic, isopropyl β -D-thiogalactoside-inducible expression vector containing the mycobacterial *FATP* gene demonstrated a significant increase in the rate of [3 H]palmitate uptake after induction, compared with uninduced bacteria or *E. coli* transformed with a control protein (Figure 4). Novel *FATP* genes were also identified in *F. rubripes* (puffer fish) and *D. melanogaster*.

Example 5: Phylogenetic Tree of FATPs

Faergeman *et al.* (Faergeman, N.J., DiRusso, C.C., Elberger, A., Knudsen, J. & Black, P. N. (1997) *J. Biol. Chem.* 272:8531-8538) identified three regions of very strong conservation between the *scFATP* and *mmFATP1* genes. The sequences of the FATPs were compared over a 311-amino acid FATP "signature sequence" which includes these conserved regions corresponding to amino acids 246-557 in *mmFATP1* (underlined in Figure 1). When compared with the National Center for Biotechnology Information nonredundant database, only one region of the "FATP signature sequence" shows significant homology to other proteins. This small stretch of amino acids (underlined in Fig. 1) is an AMP-binding motif found in a multitude of other proteins, such as acyl-CoA synthase, several CoA lipases, and gramicidin S synthetase component II (Schaffer, J.E. & Lodish, H.F. (1994) *Cell* 79:427-436). The relevance of this motif to fatty acid transport is unclear. Other highly conserved regions among the FATPs, including long stretches of amino acids >90% identical from mycobacteria to

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humans, are not found in any other class of proteins. A 48-amino acid segment of the FATP signature sequence was used to construct a phylogenetic tree (Figure 5). Each of the human and mouse genes form their own branch; hsFATP6, which as yet has no murine homologue, is most closely related to hsFATP3 and mmFATP3. As expected, mVLACS is closer in sequence to mmFATP2 than to hsFATP2. The *FATP* genes of invertebrates i.e., *C. elegans* and *D. melanogaster*, are most closely related to each other. Surprisingly, the mycobacterial gene is more closely related to the human and mouse *FATP5* genes than to the FATPs of any of the lower organisms. Whether this reflects coevolution of the mycobacterial and human genes awaits further study.

10 Materials and Methods

The following materials and methods were used in the work described in Examples 6-10.

Isolation of full-length human FATP1 and 4

Full-length clones encoding human FATP1 and human FATP4 were identified by searching databases for sequences similar to murine FATP1-5 coding regions using the BlastX algorithm (Altschul *et al.*, *J. Mol. Biol.* 215: 403-410, 1990).

A concatamer of nucleotide sequences comprising the coding sequences of mmFATP1 (Genbank Accession U15976), mmFATP2, mmFATP3 (SEQ ID NO:6), mmFATP4 (SEQ ID NO:8) and mmFATP5 (SEQ ID NO:10) was used to search the Millennium database using the BLASTX algorithm. Sequences with a score >150 were evaluated for whether they represented known FATP coding sequences.

Human clones with similarity to the 5' end of murine FATP sequences were sequenced completely. Clones encoding full-length human FATP1 were obtained from a heart cDNA library constructed in the mammalian expression vector pMET7 (Tartaglia *et al.*, *Cell*, 83: 1263-1271, 1995). Clones encoding full-length human FATP4 were obtained from a spleen cDNA library constructed in the mammalian expression vector pMET7.

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Isolation of full-length human FATP6

Several clones encoding human FATP6 were identified by searching public databases as described above. Five clones were analyzed further by restriction digestion and DNA sequencing. One of these clones (Genbank Accession # AA412064) appeared
5 to be full-length and its entire insert was sequenced.

DNA Sequence Analysis

Sequences were aligned with the DNASTar program using the Clustal method. Hydrophobicity plots were generated with DNA Strider using the Kyte Doolittle method.

10 In situ hybridization

Tissues were collected from 8 week old C57/B16 mice. Tissues were fresh frozen, cut on a cryostat at 10 μ m thickness and mounted on Superfrost Plus slides (VWR). Sections were air dried for 20 minutes and then incubated with ice cold 4% paraformaldehyde (PFA)/phosphate buffered saline (PBS) for 10 minutes. Slides were
15 washed 2 times 5 minutes with PBS, incubated with 0.25% acetic anhydride/1 M triethanolamine for 10 minutes, washed with PBS for 5 minutes and dehydrated with 70%, 80%, 95% and 100% ethanol for 1 minute each. Sections were incubated with chloroform for 5 minutes. Hybridizations were performed with 35 S-radiolabeled (5×10^7 cpm/ml) cRNA probes generated from the 3' untranslated regions of mouse FATPs by
20 PCR followed by *in vitro* transcription in the presence of 50% formamide, 10% dextran sulfate, 1x Denhardt's solution, 600 mM NaCl, 10 mM DTT, 0.25% SDS and 10 μ g/ml tRNA for 18 hours at 55°C. After hybridization, slides were washed with 10 mM Tris-HCl pH 7.6, 500 mM NaCl, 1 mM EDTA (TNE) for 10 minutes, incubated in 40 μ g/ml RNase A in TNE at 37°C for 30 minutes, washed in TNE for 10 minutes,
25 incubated once in 2x SSC at 60°C for 1 hour, once in 0.2x SSC at 60°C for 1 hour, once in 0.2x SSC at 65°C for 1 hour and dehydrated with 50%, 70%, 80%, 90% and

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100% ethanol. Localization of mRNA transcripts was detected by dipping slides in Kodak NBT-2 photoemulsion and exposing for 7 days at 4°C, followed by development with Kodak Dektol developer. Slides were counter stained with haematoxylin and eosin and photographed. Controls for the in situ hybridization experiments include the
5 use of a sense probe which showed no signal above background in all cases.

Northern Blotting

Human mRNA blots were obtained from Invitrogen or Clontech. PCR fragments from the 3' untranslated regions of human FATPs were used as probes. Blots were probed with ³²P-labeled DNA probes using the Rapid-Hyb buffer (Amersham)
10 according to the manufacturer's instructions.

Cell transfection and LCFA uptake. COS cells were cotransfected, using lipofectamine (GIBCO BRL) according to the manufacturer's instructions, with the mammalian expression vector pCDNA3.1 (Invitrogen) expressing the gene for CD2 in combination with a pMET7 expression vector (Tartaglia *et al.*, *Cell*, 83:1263-1271,
15 1995) containing hsFATP1 (pMET7-hsFATP1) or hsFATP4 (pMET7-hsFATP4) or pMET7 alone. Two days after transfection, cells were assayed for CD2 expression with a phycoerythrin-coupled anti-CD2 (PE-CD2) monoclonal antibody (PharMingen), and fatty acid uptake was assayed with a BODIPY-labeled fatty acid analog (Molecular Probes) as described above.

20 Example 6: Determination of Expression of mmFATPs

mmFATP4, and to lesser extent mmFATP2, are expressed at high levels in the brush border layer of the small intestine.

Cell transfection and LCFA uptake. COS cells were cotransfected, using lipofectamine (GIBCO BRL) according to the manufacturer's instructions, with the
25 mammalian expression vector pCDNA3.1 (Invitrogen) expressing the gene for CD2 in combination with a pMET7 expression vector (Tartaglia *et al.*, *Cell*, 83:1263-1271,

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1995) containing hsFATP1 (pMET7-hsFATP1) or hsFATP4 (pMET7-hsFATP4) or pMET7 alone. Two days after transfection, cells were assayed for CD2 expression with a phycoerythrin-coupled anti-CD2 (PE-CD2) monoclonal antibody (PharMingen), and fatty acid uptake was assayed with a BODIPY-labeled fatty acid analog (Molecular Probes) as described above.

Absorption of dietary fat requires transport of free fatty acids across the apical membrane of epithelial cells in the small intestine. Previous studies suggested that this transport is protein-mediated; however, the transport protein had not yet been identified. In situ hybridization was performed on each of the three regions of the small intestine -- duodenum, jejunum and ileum -- as well as the colon, using probes from the 3' untranslated regions of mmFATP1, mmFATP2, mmFATP3, mmFATP4 and mmFATP5, to determine whether any of the mouse FATPs are expressed in the small intestine. It was expected that a protein involved in fatty acid absorption would be expressed in the epithelial cells of the small intestine, but absent from the colon.

Expression of mmFATPs in the jejunum was identical to that in the ileum in all cases. High levels of mmFATP4 mRNA were present in the epithelial cells of the jejunum and ileum, and lower, but significant, amounts were detected in the epithelial cells of the duodenum. Significantly, FATP4 mRNA was absent from other cell types of the small intestine and no FATP4 mRNA could be detected in any of the cells of the colon. FATP2 mRNA was present in the epithelial cells of the duodenum at a level similar to that of FATP4, but was present at lower levels in the jejunum and ileum. No signals above background were detected for mmFATP1, mmFATP3 and mmFATP5 in any of the intestinal tissues. mmFATP3 and FATP5 were clearly detectable by in situ hybridization in adult liver and mmFATP1 could be detected in a variety of tissues on a whole embryo in situ, indicating that the FATP1, 3, and 5 probes were working.

mmFATP4 expression is predominant in the small intestine compared to the other organs of the mouse embryo. In the small intestine, FATP4 expression is limited to differentiated enterocytes, while no signal is detected in the connective tissue or the

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undifferentiated epithelial cells in the crypts. Differentiated enterocytes are known to be the cells that mediate the uptake of fatty acids. FATP4 is specifically and strongly expressed in the epithelial cells of adult murine duodenum and ileum but not colon. Other FATPs, such as FATP5, are not expressed in the small intestine. Thus, FATP4 is the major FATP in the mouse small intestine. Given its high level of expression, it is likely that FATP4, and to a lesser extent FATP2, play an important role in the absorption of fatty acids.

mmFATP2, and mmFATP5 are expressed in hepatocytes

Northern analysis of mmFATP2, mmFATP3, mmFATP4 and mmFATP5 showed expression in the liver. To determine whether these proteins are present in hepatocytes or other cells types present in liver homogenates, in situ hybridizations were performed. mmFATP2, and mmFATP5 mRNA was clearly present in hepatocytes, and was not concentrated in other cell types such as endothelial cells or macrophages. No signal above background was detected for mmFATP1 in any of the cell types in the liver, consistent with the results of the Northern blotting.

Example 7: Isolation and Sequence Analysis of Full-length Human FATP1 and Full-length Human FATP4

To identify human cDNA clones encoding FATP family members, Millennium databases were searched for sequences similar to murine FATP1-5 coding regions. Two clones were analyzed in detail; inspection of the entire DNA sequence of these two clones showed that they encode the human orthologs of mmFATP1 and mm FATP4, respectively. These two clones were designated hsFATP1 and hsFATP4, and their DNA and predicted protein sequences are shown in Figures 44A-44C and 45, and 50A-50C and 51. hsFATP1 is predicted to encode a 646 amino acid, 71 kD protein with multiple membrane-spanning domains (Figure 28A). HsFATP4 is predicted to encode a 643 amino acid, 72 kD protein with multiple membrane spanning domains (See Figure

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29A). A comparison of the DNA sequences of mouse and human FATP1 and mouse and human FATP4 (Figures 30A-30B and 31A-31B) shows that the mouse and human orthologs are 85% (FATP1) and 87% (FATP4) identical to each other within the coding sequences given in these figures. At the amino acid level, hsFATP1 and hsFATP4 are
 5 ~90% identical to their respective mouse orthologs within the coding region shown in these figures (Figures 32 and 33). The sequence identities between mouse and human FATP1 and FATP4 are considerably higher than the ones observed between different FATP family members within one species (~40%-60%) and are present in the N-terminal part of the protein, a region that is poorly conserved between different FATP
 10 family members. This high degree of sequence conservation clearly demonstrates that the newly identified human FATPs are orthologs of mouse FATP1 and FATP4 rather than novel FATP family members.

Table 4 is an identity/similarity matrix comparing the amino acid sequences of FATP1 and 4 from human and mouse. This shows that the gene whose sequence is
 15 shown in Figure 43A is indeed human FATP4, since it is 91% identical with the murine FATP4 but only 62% identical with the closest related human FATP, which is FATP1.

Table 4				
Identity/Similarity Matrix				
	hsFATP4	mmFATP4	hsFATP1	mmFATP1
hsFATP4	---	93.2	72.3	72.0
20 mmFATP4	91.0	---	71.2	71.1
hsFATP1	61.9	61.0	---	92.4
mmFATP1	60.7	59.6	89.5	---

Example 8: Isolation and Sequence Analysis of Full-length Human FATP6

A search of EST databases identified a set of overlapping human sequences that
 25 were similar to FATPs, but did not have a clear mouse ortholog. One of these EST

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clones was found to encode a full-length cDNA. The entire insert of this clone was sequenced and designated hsFATP6. The DNA and predicted protein sequences of hsFATP6 are shown in Figures 54A-54C and 55. HsFATP6 is predicted to encode a 619 amino acid, 70 kD protein with multiple membrane-spanning domains (Figure 35A). A comparison of the amino acid sequences of hsFATP6 with other human FATPs shows about 37% identity to either hsFATP1 or hsFATP4 (Figure 36). This degree of sequence identity is similar to what is observed between different mouse FATPs. The phylogenetic analysis described above clearly demonstrates that hsFATP6 is a member of the FATP family, but not an ortholog of any of the mouse FATPs.

10 Comparisons were done with "ALIGN" (E. Myers and W. Miller, "Optimal Alignments in Linear Space," *CABIOS* 4:11-17 (1988) using standard settings.

Example 9: Tissue Distribution of Human FATPs

The tissue distribution of human FATPs was assessed by Northern blotting. Human FATP3 was expressed in a large variety of tissues. In contrast, human FATP5 was present at high levels in the liver, but was undetectable in all other tissues examined. Thus, both hsFATP3 and hsFATP5 recapitulate the expression pattern of their mouse orthologs (see above). HsFATP6 is a novel FATP with no mouse ortholog as yet. Northern blotting shows that hsFATP6 is expressed at high levels in the heart, but is undetectable in other tissues, including skeletal and smooth muscle. This tissue distribution suggests that human FATP6 performs an important role in energy metabolism in the heart; blocking FATP6-mediated fatty acid transport may therefore be beneficial for a number of heart diseases, e.g., ischemic heart disease.

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To identify the major FATP expressed in the human small intestine, Northern blotting was performed on a blot containing mRNA from human stomach, jejunum, ileum, colon, rectum and lung. hsFATP5 and hsFATP6 were undetectable in any of these tissues. FATP5 is only expressed in liver and FATP6 only in heart. hsFATP2 was weakly expressed in the colon, and an even weaker signal was detectable in

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jejunum, ileum and lung lanes. hsFATP3 was expressed well in the lung, but was only weakly expressed in the other tissues tested. Importantly, no difference was seen in the expression of hsFATP3 between small intestine and stomach or colon, suggesting that the expression observed is not related to fatty acid absorption in the small intestine.

- 5 hsFATP4 was clearly expressed in both jejunum and ileum; expression was significantly lower in the colon and was absent in the stomach. This expression pattern is consistent with a major role for FATP4 in absorption of fatty acids in the human gut.

Example 10: Expression of hsFATP1 and hsFATP4 Promotes Transport of Fatty Acids

- COS cells were cotransfected using lipofectamine with the mammalian
10 expression vector pCDNA-CD2 in combination with one of the FATP-containing expression vectors (pMET7-hsFATP1 or pMET7-hsFATP4) or an insertless expression vector (pMET7, control) as described in Materials and Methods for Examples 6-10. COS cells were gated on forward scatter and side scatter. Cells exhibiting more than 400 CD2 fluorescence units representing ~30% of all cells were deemed CD2-positive.
15 The percent of CD2-positive cells exhibiting a BODIPY-fluorescence of >300 is plotted for the three different vectors tested (Figure 37).

Example 11: Stable Expression of Human FATP4 in 293 Cells

- Stable cell lines were generated as follows. A DNA fragment containing the entire hsFATP4 coding sequence as well as 100 nucleotides of 5' and 50 nucleotides of
20 3' untranslated region was inserted into the vector pIRES-neo (Clontech) using standard cloning techniques. The resulting construct or a vector control (pIRES-neo) was transfected into 293 cells using the lipofectamine method (Gibco BRL) according to the manufacturer's directions. Cells that had taken up the DNA were selected with 1 mg/ml G418 (Gibco BRL). Single colonies were picked 1 to 2 weeks after transfection and
25 grown in medium containing 0.8 mg/ml G418. Colonies were screened for the ability to take up fatty acids by measuring uptake of a fluorescently labeled fatty acid (BODIPY-

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FA). About 40 colonies transfected with the pIRES-neo containing FATP4 and ~20 colonies transfected with pIRES-neo control were analyzed. All 20 of the vector control clones showed amounts of BODIPY-FA uptake similar to each other and to untransfected 293 cells. In contrast, among the 40 FATP4 transfected clones, 3 had a 5- to 10-fold increased BODIPY-FA uptake compared to any of the vector controls, and a large number (~20) showed an approximately two-fold increase in BODIPY-FA levels. This distribution is consistent with FATP4 conferring increased fatty acid uptake in these cells. One of the cell lines with the highest amount of BODIPY-FA uptake was selected to be used for measuring uptake of tritiated fatty acid.

10 The uptake of tritiated oleate over time by either FATP4 expressing or control cells was assayed over time. Expression of FATP4 increases the rate of fatty acid uptake by over 3-fold, demonstrating that FATP4 is, like the other FATPs, a functional fatty acid transporter (Figure 38).

Example 12: Immuno-staining with FATP4-Specific Antiserum

15 A polyclonal antiserum against the C-terminus of mmFATP4 was raised using a GST-fusion protein having mmFATP4-specific amino acid sequence 552-643 (AVASP...GEEKL). In western blot experiments, the purified antibody reacted strongly with a synthetic peptide matching the C-terminus of mmFATP4, but not with a corresponding region of mmFATP2, mmFATP3, or mmFATP5. The mmFATP4 specific polyclonal antiserum detects, in western blot experiments with enterocyte lysates from 3 different mice, a ~70 kDa protein, which is in accordance with mmFATP4's predicted molecular weight of 72 kDa. The binding is specific for mmFATP4, since it can be completely abolished by preincubation of the antiserum with the GST-fusion peptide used to raise the antibody.

25 Immunofluorescence experiments were performed using the anti-mmFATP4 antiserum on fresh frozen sections of murine small intestine. The antibody binding demonstrates strong expression of mmFATP4 in enterocytes, confirming the results of

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the in situ hybridization experiments. At higher magnifications it is apparent that mmFATP4 is expressed at the apical side of the enterocyte, indicating that the transporter is present in the brush border membrane, which is known to mediate the uptake of fatty acids from the intestinal lumen.

- 5 Immuno-electron microscopy studies were performed on fresh frozen murine intestinal cells. The gold particles used, appearing as black specks on the electron micrographs, indicate the subcellular localization of mmFATP4 to be on the microvilli of the enterocyte. It can be seen from the electron micrographs that mmFATP4 is localized exclusively in membranes, preferentially the apical plasma membrane,
10 confirming that it is indeed a membrane protein.

Example 13: Inhibition of Fatty Acid Uptake Specific to FATP4 Demonstrated in Isolated Mouse Enterocytes

Phosphorothioate derivatives of the following oligonucleotides were synthesized:

- | | | |
|----|-------------|-------------------------------------|
| 15 | FATP4-AS2 | CCCCCACCAGAGAGGCTCC (SEQ ID NO:100) |
| | FATP4-AS2MM | CCACCCCCGGAAAGCCTGC (SEQ ID NO:101) |
| | FATP4-S2 | GGAGCCTCTCTGGTGGGGG (SEQ ID NO:102) |

FATP4 AS2 is the antisense oligo; it is designed to be complementary to the sequence extending from nucleotide 10 to nucleotide 28 of the mouse FATP4 coding sequence.

- 20 FATP4-AS2MM is a control oligo; in the oligo every third nucleotide was changed creating mismatches; the overall nucleotide composition is identical to FATP4-AS2 (same number of G, A, T, C). FATP4-S2 is the sense control.

Enterocytes were isolated from the small intestine of mice and incubated for 48h in tissue culture (Figure 40) either without oligonucleotides (squares) or with 100 μ M

- 25 FATP4 specific sense (circles) or antisense (diamonds) oligonucleotides. The uptake over time of 25 μ M oleate was then measured. While the FATP4 sense oligonucleotide

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did not significantly influence the uptake, the antisense oligonucleotide inhibited fatty acid uptake by ~50%.

The effect of either FATP4 sense, antisense or mismatch sequence oligonucleotides on the uptake of fatty acids was measured in enterocytes. Isolated enterocytes were incubated with increasing concentrations of FATP4 antisense oligonucleotides (solid bars in Figure 41), or a mismatch control oligonucleotide with identical nucleotide composition (stippled bars), or with 100 μ M of the FATP4 sense-oligonucleotide (lined bar). The medium for this incubation was Dulbecco's modified Eagle's medium with 4.5 g/L glucose, 1 mM sodium pyruvate, 0.01 mg/ml human transferrin and 10% fetal bovine serum. After 48 hours of incubation the uptake of oleate by enterocytes was measured over a 5 minute time interval. Measurements were done in quadruplicate. The uptake assay was done in Hank's buffered salt solution with 10 mM taurocholate. Only the enterocytes given FATP4 antisense oligonucleotide showed a concentration dependent decrease of fatty acid uptake, inhibiting it at a 100 μ M concentration by ~50%. This effect was FATP4 specific, since only the antisense oligonucleotide which can bind to the FATP4 mRNA and block its translation inhibited uptake, but not a control oligonucleotide differing only in the sequence but not the nucleotide content, ruling out a toxic or otherwise nonspecific inhibitory effect of this oligonucleotide due to its chemical composition.

As a further control experiment, the uptake of oleate was measured along with the uptake of methionine in the same cultured enterocytes. Antisense oligonucleotide, mismatch sequence oligonucleotide, or no oligonucleotide was added to a concentration of 100 μ M to cultures of enterocytes. After incubation for 48 hours, the uptake of both 3 H-labeled oleate and 35 S-labeled methionine was assayed. Results are shown in Figure 42. Fatty acid uptake is at the left side of the paired bars; methionine uptake is on the right side of the paired bars. The fact that amino acid uptake was not influenced by the antisense oligonucleotide treatment further supports the conclusion that the antisense oligonucleotide causes a specific reduction in translation of FATP4-specific mRNA.

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Example 14: mmFATP2 Is Expressed in Proximal Renal Tubule Epithelium

Northern analysis showed that mmFATP1, mmFATP2, and mmFATP4 are present in the kidney. In situ hybridization (methods as for Example 6) was performed to determine which cell type(s) of the kidney these mRNAs are expressed in.

- 5 mmFATP1 mRNA was present in virtually all cells throughout the kidney with no obvious preference for a particular cell type. In contrast, mmFATP2 was expressed only in the renal cortex. Within the cortex, expression of mmFATP2 was restricted to the epithelial cells of the proximal renal tubules. The primary function of proximal renal tubule cells is the reabsorption of filtered salts and nutrients (e.g., glucose), a
- 10 process that requires mitochondrial oxidation and that can utilize fatty acids as energy substrates. Based on the localization of mmFATP2, it is possible that mmFATP2 is important for reabsorption in the kidney by allowing uptake of an energy source (fatty acids) from the blood into renal epithelial cells. Alternatively, if fatty acids need to be reabsorbed in the kidney, similarly to glucose, FATP2 could be involved in the
- 15 reabsorption of fatty acids. Determination of the subcellular localization of FATP2 will distinguish between these two possibilities.

Table 5 summarizes data on expression of the mouse FATPs in various organs.

Table 5. Mouse FATP mRNA Expression

Mouse Probes	mFATP1	mFATP2	mFATP3	mFATP4	mFATP5
E18.5 embryo expression	everywhere, brain = thymus> heart> brown fat, others	liver (hepatocytes)	-	Brain, small intestine, superior cervical ganglion (SCG), dorsal root ganglion (DRG), other regions have lower expression	Mouse Probes
Duodenum	-	villi (surface epithelium)	-	villi (surface epithelium)	-
Jejunum	-	villi (surface epithelium)	-	villi (surface epithelium)	-
Ileum	-	villi (surface epithelium)	-	villi (surface epithelium)	-
Colon	low expression in the crypt	very low level in the crypt	-	-	-
Kidney	cortex and medulla	proximal tubules	-	-	-

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Table 5 (continued). Mouse FATP mRNA Expression

Mouse Probes	mFATP1	mFATP2	mFATP3	mFATP4	mFATP5
Liver	-	hepatocytes	hepatocytes	-	hepatocytes
Pancreas	exocrine secretory units or acinar cells; endocrine pancreas (islet) are negative	exocrine secretory units or acinar cells; endocrine pancreas (islet) are negative	-	-	-
Brain	Neuronal expression throughout the brain including hypothalamus	-	-	Neuronal expression throughout the brain including hypothalamus	-
Heart	myocytes	-	-		
Testis	seminiferous tubules	-	seminiferous tubules		
Lung	bronchiole	-	-		
Adipose	adipocyte	adipocyte	-		

Example 15: Isolation of full-length human FATP3

Full-length clones encoding human FATP3 were identified by searching databases for sequences similar to the murine FATP1-5 coding regions using the BlastX algorithm (Altschul *et al.*, *J. Mol. Biol.* 215: 403-410, 1990). Human clones with
5 similarity to the 5' end of murine FATP sequences were sequenced completely. A clone encoding full-length human FATP3 was obtained from a human bone library constructed in the mammalian expression vector pMET7 (Tartaglia, L.A. *et al.*, *Cell* 83: 1263-1271, 1995). To identify human cDNA clones encoding FATP family members, databases were searched for sequences similar to murine FATP1-5 coding regions. One
10 clone was found to encode the human ortholog of mmFATP3 and was designated hsFATP3. The DNA and predicted protein sequences of hsFATP3 are shown in Figures 94A and 94B. hsFATP3 is predicted to encode a 703 amino acid 75.6 kD protein with multiple membrane-spanning domains. A comparison of the DNA sequences of mouse and human FATP3 shows that the mouse and human orthologs are 81% identical to
15 each other within the coding region. At the amino acid level, hsFATP3 is ~86% identical to mm FATP3 within the coding region. The sequence identities between mouse and human FATP3 are considerably higher than those observed between different FATP family members within one species (~40%) and are present in the N-terminal part of the protein, a region that is poorly conserved between different FATP
20 family members.

All references cited herein are incorporated by reference in their entirety.

While this invention has been particularly shown and described with references to preferred embodiments thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the
25 spirit and scope of the invention as defined by the appended claims.

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CLAIMS

What is claimed is:

1. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
 - 5 a) a nucleotide sequence which encodes a protein consisting of the amino acid sequence of FATP2 in SEQ ID NO:49;
 - b) a nucleotide sequence which encodes a protein consisting of the amino acid sequence of FATP4 in SEQ ID NO:53; and
 - 10 c) a nucleotide sequence which encodes a protein consisting of the amino acid sequence of FATP6 in SEQ ID NO:57.
2. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
 - a) the nucleotide sequence in SEQ ID NO:48;
 - b) the nucleotide sequence in SEQ ID NO:52; and
 - 15 c) the nucleotide sequence in SEQ ID NO:56.
3. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
 - a) a nucleotide sequence which is complementary to the nucleotide sequence of FATP2 in SEQ ID NO:48;
 - 20 b) a nucleotide sequence which is complementary to the nucleotide sequence of FATP4 in SEQ ID NO:52; and
 - c) a nucleotide sequence which is complementary to the nucleotide sequence of FATP6 in SEQ ID NO:56.

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4. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
- a) a nucleotide sequence which consists of the coding region of FATP2;
 - b) a nucleotide sequence which consists of the coding region of FATP4;
 - 5 and
 - c) a nucleotide sequence which consists of the coding region of FATP6.
5. An isolated nucleic acid molecule comprising at least 15 contiguous nucleotides of a nucleotide sequence selected from the group consisting of :
- a) SEQ ID NO:48, or of the complement thereof;
 - 10 b) SEQ ID NO:52, or of the complement thereof; and
 - c) SEQ ID NO:56, or of the complement thereof.
6. An isolated nucleic acid molecule comprising a nucleotide sequence which encodes a contiguous portion of at least about 15 amino acids of a sequence selected from the group consisting of SEQ ID NO:48, SEQ ID NO:52, and SEQ
- 15 ID NO:56.
7. An isolated nucleic acid molecule comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of a fatty acid transport protein, wherein said nucleic acid molecule hybridizes under high stringency conditions to a complement of a
- 20 sequence selected from the group consisting of SEQ ID NO:48, SEQ ID NO:52, and SEQ ID NO:56.
8. An isolated nucleic acid molecule having at least 90% nucleotide sequence identity to a nucleic acid encoding a polypeptide comprising an amino acid

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sequence selected from the group consisting of SEQ ID NO:49, SEQ ID NO:53, and SEQ ID NO:57.

9. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide, wherein said nucleotide sequence is at least 95% similar to the nucleotide sequence of a nucleotide sequence selected from the group consisting of SEQ ID NO:48, SEQ ID NO:52, and SEQ ID NO:56.
5
10. An isolated nucleic acid encoding a fatty acid transport protein having an amino acid sequence sharing at least about 95% amino acid sequence similarity with an amino acid sequence selected from the group consisting of SEQ ID NO:49, SEQ ID NO:53, and SEQ ID NO:57.
10
11. An isolated nucleic acid molecule encoding a fusion polypeptide, said nucleic acid molecule comprising a nucleotide sequence encoding a portion of an amino acid sequence selected from the group consisting of SEQ ID NO:49, SEQ ID NO:53, and SEQ ID NO:57, and further comprising a nucleotide sequence encoding a heterologous portion of said fusion polypeptide.
15
12. A vector comprising a nucleic acid comprising a nucleotide sequence selected from the group consisting of:
 - a) a nucleotide sequence which encodes a protein comprising the amino acid sequence of FATP2 in SEQ ID NO:49;
 - 20 b) a nucleotide sequence which encodes a protein comprising the amino acid sequence of FATP4 in SEQ ID NO:53; and
 - c) a nucleotide sequence which encodes a protein comprising the amino acid sequence of FATP6 in SEQ ID NO:57.

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13. A vector comprising a nucleic acid comprising a nucleotide sequence selected from the group consisting of:
- a) the nucleotide sequence of FATP2 in SEQ ID NO:48;
 - b) the nucleotide sequence of FATP4 in SEQ ID NO:52; and
 - 5 c) the nucleotide sequence of FATP6 in SEQ ID NO:56.
14. A vector comprising a nucleic acid comprising a nucleotide sequence selected from the group consisting of:
- a) a nucleotide sequence which is complementary to the nucleotide sequence of FATP2 in SEQ ID NO:48;
 - 10 b) a nucleotide sequence which is complementary to the nucleotide sequence of FATP4 in SEQ ID NO:52; and
 - c) a nucleotide sequence which is complementary to the nucleotide sequence of FATP6 in SEQ ID NO:56.
15. A vector comprising a nucleic acid comprising a nucleotide sequence selected from the group consisting of:
- a) a nucleotide sequence which consists of the coding region of FATP2;
 - b) a nucleotide sequence which consists of the coding region of FATP4; and
 - c) a nucleotide sequence which consists of the coding region of FATP6.
- 20 16. A host cell comprising the vector of Claim 15.
17. An isolated nucleic acid molecule comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of a fatty acid transport protein, wherein said nucleic acid molecule hybridizes under high stringency conditions to a complement of a

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nucleic acid molecule consisting of a sequence selected from the group consisting of SEQ ID NO:48, SEQ ID NO:52, and SEQ ID NO: 56.

18. A vector comprising a nucleic acid comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of a fatty acid transport protein, wherein said nucleic acid molecule hybridizes under high stringency conditions to a complement of a nucleic acid molecule consisting of a sequence selected from the group consisting of SEQ ID NO:48, SEQ ID NO:52, and SEQ ID NO:56.
19. A host cell comprising the vector of Claim 8.
20. A method for producing a polypeptide which is a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of a fatty acid transport protein, said method comprising culturing the host cell of Claim 19 under conditions in which the nucleic acid molecule is expressed, thereby producing the polypeptide.
21. A vector comprising a nucleic acid having at least 90% nucleotide sequence identity to a nucleic acid encoding a polypeptide consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:49, SEQ ID NO:53, and SEQ ID NO:57.
22. A host cell comprising the vector of Claim 21.
23. A method for producing a polypeptide, said method comprising culturing the host cell of Claim 22 under conditions in which the nucleic acid molecule is expressed, thereby producing the polypeptide.

24. A vector comprising a nucleic acid encoding a fatty acid transport protein having an amino acid sequence sharing at least about 95% amino acid sequence similarity with an amino acid sequence selected from the group consisting of SEQ ID NO:49, SEQ ID NO:53, and SEQ ID NO:57.
- 5 25. A host cell comprising the vector of Claim 24.
26. A method for producing a fatty acid transport protein, said method comprising culturing the host cell of Claim 25 under conditions in which the nucleic acid molecule is expressed, thereby producing the fatty acid transport protein.
- 10 27. A vector comprising a nucleic acid encoding a fusion polypeptide, said nucleic acid comprising a nucleotide sequence which encodes a contiguous portion of at least about 15 amino acids of a sequence selected from the group consisting of SEQ ID NO:49, SEQ ID NO:53, and SEQ ID NO:57.
28. A host cell comprising the vector of Claim 27.
- 15 29. A method for producing a fusion polypeptide, said method comprising culturing the host cell of Claim 28 under conditions in which the nucleic acid is expressed, thereby producing the fusion polypeptide.
30. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
- 20 a) a nucleotide sequence which encodes a protein consisting of the amino acid sequence of FATP1 in SEQ ID NO:47;
- b) a nucleotide sequence which encodes a protein consisting of the amino acid sequence of FATP3 in SEQ ID NO:51; and

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- c) a nucleotide sequence which encodes a protein consisting of the amino acid sequence of FATP5 in SEQ ID NO:102.
31. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
- 5 a) the nucleotide sequence in SEQ ID NO:46;
- b) the nucleotide sequence in SEQ ID NO:50; and
- c) the nucleotide sequence in SEQ ID NO:101.
32. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
- 10 a) a nucleotide sequence which is complementary to the nucleotide sequence of FATP1 in SEQ ID NO:46;
- b) a nucleotide sequence which is complementary to the nucleotide sequence of FATP3 in SEQ ID NO:50; and
- 15 c) a nucleotide sequence which is complementary to the nucleotide sequence of FATP5 in SEQ ID NO:101.
33. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
- a) a nucleotide sequence which consists of the coding region of FATP1;
- b) a nucleotide sequence which consists of the coding region of FATP3;
- 20 and
- c) a nucleotide sequence which consists of the coding region of FATP5.
34. An isolated nucleic acid molecule comprising at least 15 contiguous nucleotides of a nucleotide sequence selected from the group consisting of:
- a) SEQ ID NO:46, or of the complement thereof;

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- b) SEQ ID NO:50, or of the complement thereof; and
 - c) SEQ ID NO:101, or of the complement thereof.
35. An isolated nucleic acid molecule comprising a nucleotide sequence which encodes a contiguous portion of at least about 15 amino acids of a sequence selected from the group consisting of SEQ ID NO:47, SEQ ID NO:51, and SEQ ID NO:102.
36. An isolated nucleic acid molecule comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of a fatty acid transport protein, wherein said nucleic acid molecule hybridizes under high stringency conditions to a complement of a sequence selected from the group consisting of SEQ ID NO:46, SEQ ID NO:50, and SEQ ID NO:101.
37. An isolated nucleic acid molecule having at least 90% nucleotide sequence identity to a nucleic acid encoding a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:47, SEQ ID NO:51, and SEQ ID NO:102.
38. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide, wherein said nucleotide sequence is at least 90% identical to the nucleotide sequence of a nucleotide sequence selected from the group consisting of SEQ ID NO:46, SEQ ID NO:50, and SEQ ID NO:101, and wherein said percent identity is calculated using the GAP program in the GCG software package, using a gap weight of 5.000 and a length weight of 0.100.

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39. An isolated nucleic acid encoding a fatty acid transport protein having an amino acid sequence sharing at least about 95% amino acid sequence similarity with an amino acid sequence selected from the group consisting of SEQ ID NO:47, SEQ ID NO:51, and SEQ ID NO:102.
- 5 40. An isolated nucleic acid molecule encoding a fusion polypeptide, said nucleic acid molecule comprising a nucleotide sequence encoding a portion of an amino acid sequence selected from the group consisting of SEQ ID NO:47, SEQ ID NO:51, and SEQ ID NO:102, and further comprising a nucleotide sequence encoding a heterologous portion of said fusion polypeptide.
- 10 41. A vector comprising a nucleic acid comprising a nucleotide sequence selected from the group consisting of:
- a) a nucleotide sequence which encodes a protein comprising the amino acid sequence of FATP1 in SEQ ID NO:47;
 - b) a nucleotide sequence which encodes a protein comprising the amino acid sequence of FATP3 in SEQ ID NO:51; and
 - 15 c) a nucleotide sequence which encodes a protein comprising the amino acid sequence of FATP5 in SEQ ID NO:102.
42. A vector comprising a nucleic acid comprising a nucleotide sequence selected from the group consisting of:
- 20 a) the nucleotide sequence of FATP1 in SEQ ID NO:46;
 - b) the nucleotide sequence of FATP3 in SEQ ID NO:50; and
 - c) the nucleotide sequence of FATP5 in SEQ ID NO:101.
43. A vector comprising a nucleic acid comprising a nucleotide sequence selected from the group consisting of:

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- 5 a) a nucleotide sequence which is complementary to the nucleotide sequence of FATP1 in SEQ ID NO:46;
- b) a nucleotide sequence which is complementary to the nucleotide sequence of FATP3 in SEQ ID NO:50; and
- c) a nucleotide sequence which is complementary to the nucleotide sequence of FATP5 in SEQ ID NO:101.
44. A vector comprising a nucleic acid comprising a nucleotide sequence selected from the group consisting of:
- 10 a) a nucleotide sequence which consists of the coding region of FATP1;
- b) a nucleotide sequence which consists of the coding region of FATP3; and
- c) a nucleotide sequence which consists of the coding region of FATP5.
45. A host cell comprising the vector of Claim 44.
- 15 46. An isolated nucleic acid molecule comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of a fatty acid transport protein, wherein said nucleic acid molecule hybridizes under high stringency conditions to a complement of a nucleic acid molecule consisting of a sequence selected from the group consisting of SEQ ID NO:46, SEQ ID NO:50, and SEQ ID NO:101.
- 20 47. A vector comprising a nucleic acid comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of a fatty acid transport protein, wherein said nucleic acid molecule hybridizes under high stringency conditions to a complement of a

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nucleic acid molecule consisting of a sequence selected from the group consisting of SEQ ID NO:46, SEQ ID NO:50, and SEQ ID NO:101.

48. A host cell comprising the vector of Claim 47.
49. A method for producing a polypeptide which is a naturally occurring allelic
5 variant of a polypeptide consisting of the amino acid sequence of a fatty acid
transport protein, said method comprising culturing the host cell of Claim 48
under conditions in which the nucleic acid molecule is expressed, thereby
producing the polypeptide.
50. A vector comprising a nucleic acid having at least 90% nucleotide sequence
10 identity to a nucleic acid encoding a polypeptide consisting of an amino acid
sequence selected from the group consisting of SEQ ID NO:47, SEQ ID NO:51,
and SEQ ID NO:102.
51. A host cell comprising the vector of Claim 50.
52. A method for producing a polypeptide, said method comprising culturing the
15 host cell of Claim 51 under conditions in which the nucleic acid molecule is
expressed, thereby producing the polypeptide.
53. A vector comprising a nucleic acid encoding a fatty acid transport protein having
an amino acid sequence sharing at least about 95% amino acid sequence
similarity with an amino acid sequence selected from the group consisting of
20 SEQ ID NO:47, SEQ ID NO:51, and SEQ ID NO:102.
54. A host cell comprising the vector of Claim 53.

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55. A method for producing a fatty acid transport protein, said method comprising culturing the host cell of Claim 54 under conditions in which the nucleic acid molecule is expressed, thereby producing the fatty acid transport protein.
- 5 56. A vector comprising a nucleic acid encoding a fusion polypeptide, said nucleic acid comprising the nucleotide sequence which encodes a contiguous portion of at least about 15 amino acids of a sequence selected from the group consisting of SEQ ID NO:47, SEQ ID NO:51, and SEQ ID NO:102, said nucleic acid further comprising a nucleotide sequence encoding a heterologous portion of said fusion polypeptide.
- 10 57. A host cell comprising the vector of Claim 56.
58. A method for producing a fusion polypeptide, said method comprising culturing the host cell of Claim 57 under conditions in which the nucleic acid is expressed, thereby producing the fusion polypeptide.
59. Isolated FATP2 or a functional portion thereof.
- 15 60. An isolated polypeptide comprising an amino acid sequence which is at least 90% identical to the amino acid sequence of SEQ ID NO:49.
61. An isolated polypeptide comprising an amino acid sequence which is at least 95% identical to the amino acid sequence of SEQ ID NO:49.
62. An isolated polypeptide comprising an amino acid sequence which is at least 97% identical to the amino acid sequence of SEQ ID NO:49.
- 20

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63. Isolated polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP2, wherein said nucleic acid molecule hybridizes to a complement of a nucleic acid molecule consisting of SEQ ID NO:48 under high stringency conditions.
64. An isolated polypeptide comprising an amino acid sequence in SEQ ID NO:49.
65. A fusion protein comprising a polypeptide or peptide selected from the group consisting of:
- a) a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP2 in SEQ ID NO:49;
 - b) a polypeptide consisting of an amino acid sequence which is at least 95% identical to the amino acid sequence of SEQ ID NO:49;
 - c) a polypeptide consisting of an amino acid sequence in SEQ ID NO:49; and
 - d) a peptide comprising a contiguous portion of at least about 15 amino acid residues of any of the foregoing.
66. The fusion protein of Claim 65 wherein the fusion protein transports fatty acids across a cell membrane or an artificial cell membrane system.
67. The fusion protein of Claim 65, further comprising an affinity ligand.
68. Isolated FATP4 or a functional portion thereof.
69. An isolated polypeptide comprising an amino acid sequence which is at least 90% identical to the amino acid sequence of SEQ ID NO:53.

70. An isolated polypeptide comprising an amino acid sequence which is at least 95% identical to the amino acid sequence of SEQ ID NO:53.
71. An isolated polypeptide comprising an amino acid sequence which is at least 97% identical to the amino acid sequence of SEQ ID NO:53.
- 5 72. Isolated polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP4, wherein said nucleic acid molecule hybridizes to a complement of a nucleic acid molecule consisting of SEQ ID NO:52 under high stringency conditions.
- 10 73. An isolated polypeptide comprising an amino acid sequence in SEQ ID NO:53.
74. A fusion protein comprising a polypeptide or peptide selected from the group consisting of:
- a) a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP4 in SEQ ID NO:53;
 - 15 b) a polypeptide consisting of an amino acid sequence which is at least 95% identical to the amino acid sequence of SEQ ID NO:53;
 - c) a polypeptide consisting of an amino acid sequence in SEQ ID NO:53; and
 - d) a peptide comprising a contiguous portion of at least about 15 amino acid
- 20 residues of any of the foregoing.
75. The fusion protein of Claim 74 wherein the fusion protein transports fatty acids across a cell membrane or an artificial cell membrane system.

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76. The fusion protein of Claim 74, further comprising an affinity ligand.
77. Isolated FATP6 or a functional portion thereof.
78. An isolated polypeptide comprising an amino acid sequence which is at least 90% identical to the amino acid sequence of SEQ ID NO:57.
- 5 79. An isolated polypeptide comprising an amino acid sequence which is at least 95% identical to the amino acid sequence of SEQ ID NO:57.
80. An isolated polypeptide comprising an amino acid sequence which is at least 97% identical to the amino acid sequence of SEQ ID NO:57.
- 10 81. Isolated polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP6, wherein said nucleic acid molecule hybridizes to a complement of a nucleic acid molecule consisting of SEQ ID NO:56 under high stringency conditions.
82. An isolated polypeptide comprising an amino acid sequence in SEQ ID NO:57.
- 15 83. A fusion protein comprising a polypeptide or peptide selected from the group consisting of:
- a) a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP6 in SEQ ID NO:57;
 - b) a polypeptide consisting of an amino acid sequence which is at least 95% identical to the amino acid sequence of SEQ ID NO:57;
- 20

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- c) a polypeptide consisting of an amino acid sequence in SEQ ID NO:57;
and
- d) a peptide comprising a contiguous portion of at least about 15 amino acid residues of any of the foregoing.

5 84. The fusion protein of Claim 83 wherein the fusion protein transports fatty acids across a cell membrane or an artificial cell membrane system.

85. The fusion protein of Claim 83, further comprising an affinity ligand.

86. A method for identifying an agent which binds to a protein comprising an amino acid sequence of SEQ ID NO:49 or SEQ ID NO:53, comprising the steps of
10 contacting the agent with the isolated protein under conditions appropriate for binding of the agent to the isolated protein, and detecting a resulting agent-protein complex.

87. The method of Claim 86 wherein the step of contacting the agent with isolated protein is performed in an artificial membrane system.

15 88. The method of Claim 86 wherein the isolated protein is in isolated plasma membrane.

89. A method for identifying an agent which inhibits interaction between an isolated protein comprising amino acid sequence SEQ ID NO:49, or SEQ ID NO:53, and further comprising a ligand of said protein, comprising:

- 20 (a) combining:
- (1) said isolated protein;
 - (2) the ligand of said protein; and

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- (3) a candidate agent to be assessed for its ability to inhibit interaction between said protein of (1) and the ligand of (2), under conditions appropriate for interaction between the said protein of (1) and the ligand of (2);
- 5 (b) determining the extent to which said protein of (1) and the ligand of (2) interact; and
- (c) comparing the extent determined in (b) with the extent to which interaction of said protein of (1) and the ligand of (2) occurs in the absence of the candidate agent to be assessed and under the same
- 10 conditions appropriate for interaction of said protein of (1) with the ligand of (2);
- wherein if the extent to which interaction of said protein of (1) and the ligand of (2) occurs is less in the presence of the candidate agent than in the absence of the candidate agent, the candidate agent is an agent which inhibits interaction
- 15 between said protein and the ligand of said protein.
90. The method of Claim 89 wherein (a) is performed in an artificial membrane system.
91. The method of Claim 89 wherein said isolated protein is in isolated plasma membrane.
- 20 92. A method for identifying an agent which binds to a protein, said protein encoded by (1) a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP2, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:48 under high stringency conditions,
- 25 or by (2) a polynucleotide comprising a nucleotide sequence which encodes a

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5 naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP4, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:52 under high stringency conditions, comprising the steps of isolating the protein, contacting the agent with the isolated protein under conditions appropriate for binding of the agent to the isolated protein, and detecting a resulting agent-protein complex.

93. The method of Claim 92 wherein the step of contacting the agent with the isolated protein is performed in an artificial membrane system.

10 94. The method of Claim 92 wherein the isolated protein is in isolated plasma membrane.

15 95. A method for identifying an agent which inhibits interaction between (1) an isolated protein, said protein being encoded by (i) a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP2, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:48 under high stringency conditions, or by (ii) a polynucleotide having a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP4, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of
20 SEQ ID NO:52 under high stringency conditions and (2) a ligand of said protein, comprising:

(a) combining:

- (1) said isolated protein;
- (2) the ligand of said protein; and

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- (3) a candidate agent to be assessed for its ability to inhibit interaction between said protein of (1) and the ligand of (2), under conditions appropriate for interaction between said protein of (1) and the ligand of (2);
- 5 (b) determining the extent to which said protein of (1) and the ligand of (2) interact; and
- (c) comparing the extent determined in (b) with the extent to which interaction of said protein of (1) and the ligand of (2) occurs in the absence of the candidate agent to be assessed and under the same
- 10 conditions appropriate for interaction of said protein of (1) with the ligand of (2);
- wherein if the extent to which interaction of said protein of (1) and the ligand of (2) occurs is less in the presence of the candidate agent than in the absence of the candidate agent, the candidate agent is an agent which inhibits interaction
- 15 between said protein and the ligand of said protein.
96. The method of Claim 95 wherein (a) is performed in an artificial membrane system.
97. The method of Claim 95 wherein said isolated protein is in isolated plasma membrane.
- 20 98. A method for identifying an agent which binds to a protein encoded by a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:49, or SEQ ID NO:53 comprising the steps of isolating the protein, contacting the agent with the isolated protein under conditions

appropriate for binding of the agent to the isolated protein, and detecting a resulting agent-protein complex.

99. The method of Claim 98 wherein the step of contacting the agent with isolated protein is performed in an artificial membrane system.
- 5 100. The method of Claim 98 wherein the isolated protein is in isolated plasma membrane.
101. A method for identifying an agent which inhibits interaction between (i) an isolated protein encoded by a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 90% amino acid
10 sequence similarity with the amino acid sequence in SEQ ID NO:49, or (ii) a protein encoded by a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 90% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:53 and a ligand of said protein, said method comprising:
- 15 (a) combining:
- (1) said isolated protein;
- (2) the ligand of said protein; and
- (3) a candidate agent to be assessed for its ability to inhibit
interaction between said protein of (1) and the ligand of (2),
20 under conditions appropriate for interaction between the said protein of (1) and the ligand of (2);
- (b) determining the extent to which said protein of (1) and the ligand of (2) interact; and
- (c) comparing the extent determined in (b) with the extent to which
25 interaction of said protein of (1) and the ligand of (2) occurs in the

absence of the candidate agent to be assessed and under the same conditions appropriate for interaction of said protein of (1) with the ligand of (2);

5 wherein if the extent to which interaction of said protein of (1) and the ligand of (2) occurs is less in the presence of the candidate agent than in the absence of the candidate agent, the candidate agent is an agent which inhibits interaction between said protein and the ligand of said protein.

102. The method of Claim 101 wherein (a) is performed in an artificial membrane system.

10 103. The method of Claim 101 wherein said isolated protein is in isolated plasma membrane.

104. A method for identifying an agent which is an inhibitor of fatty acid uptake by (i) a protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a protein consisting of the amino acid sequence in SEQ ID
15 NO:49, or by (ii) a protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a protein consisting of the amino acid sequence in SEQ ID NO:53, comprising the steps of:

- a) maintaining test cells expressing said polynucleotide in the presence of a fatty acid and an agent to be tested as an inhibitor of fatty acid uptake;
- 20. b) measuring uptake of the fatty acid in the test cells; and
- c) comparing uptake of the fatty acid in the test cells with uptake of the fatty acid in suitable control cells;

wherein lower uptake of the fatty acid in the test cells compared to uptake of the fatty acid in the control cells is indicative that the agent is an inhibitor of fatty
25 acid uptake by said protein.

105. An inhibitor of fatty acid uptake identified by the method of Claim 104.
106. The method of Claim 104 further comprising the steps of:
- a) administering the agent to one or more test animals;
 - b) measuring exogenously supplied fatty acids in one or more samples of
5 tissue or bodily fluid from said test animals;
 - c) measuring exogenously supplied fatty acids in one or more comparable
samples of tissue or bodily fluid from suitable control animals;
 - d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is
10 an inhibitor of said protein.
107. An inhibitor of fatty acid uptake identified by the method of Claim 106.
108. A method for identifying an agent which is an inhibitor of fatty acid uptake by a
protein, said protein encoded by (i) a polynucleotide comprising a nucleotide
sequence which encodes a naturally occurring allelic variant of a polypeptide
15 consisting of the amino acid sequence of FATP2, wherein said polynucleotide
hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:48
under high stringency conditions, or by (ii) a polynucleotide comprising a
nucleotide sequence which encodes a naturally occurring allelic variant of a
polypeptide consisting of the amino acid sequence of FATP4, wherein said
20 polynucleotide hybridizes to a complement of a polynucleotide consisting of
SEQ ID NO:52 under high stringency conditions, comprising the steps of:
- a) maintaining test cells expressing said polynucleotide in the presence of a
fatty acid and an agent to be tested as an inhibitor of fatty acid uptake;
 - b) measuring uptake of the fatty acid in the test cells; and

- c) comparing uptake of the fatty acid in the test cells with uptake of the fatty acid in suitable control cells;

wherein lower uptake of the fatty acid in the test cells compared to uptake of the fatty acid in the control cells is indicative that the agent is an inhibitor of fatty acid uptake by said protein.

109. An inhibitor of fatty acid uptake identified by the method of Claim 108.

110. The method of Claim 108 further comprising the steps of:

- a) administering the agent to one or more test animals;
b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from said test animals;
c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals;
d) comparing the fatty acids of b) with the fatty acids of c);

whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

111. An inhibitor of fatty acid uptake identified by the method of Claim 110.

112. A method for identifying an agent which is an inhibitor of fatty acid uptake by a protein, said protein being encoded by (i) a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:49 or by (ii) a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:53, comprising the steps of:

- a) maintaining test cells expressing said polynucleotide in the presence of a fatty acid and an agent to be tested as an inhibitor of fatty acid uptake;
- b) measuring uptake of the fatty acid in the test cells; and
- c) comparing uptake of the fatty acid in the test cells with uptake of the fatty acid in suitable control cells;

5

wherein lower uptake of the fatty acid in the test cells compared to uptake of the fatty acid in the control cells is indicative that the agent is an inhibitor of fatty acid uptake by said protein.

113. An inhibitor of fatty acid uptake identified by the method of Claim 112.

10 114. The method of Claim 112 further comprising the steps of:

- a) administering the agent to one or more test animals;
- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from said test animals;
- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals;
- d) comparing the fatty acids of b) with the fatty acids of c);

15

whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

115. An inhibitor of fatty acid uptake identified by the method of Claim 114.

20 116. A method for identifying an agent which is an inhibitor of (i) a protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a protein comprising the amino acid sequence in SEQ ID NO:49 or (ii) a protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a protein comprising the amino acid sequence in SEQ ID NO:53, comprising the steps of:

- (a) introducing into host cells one or more vectors comprising a polynucleotide expressing said protein;
- (b) culturing a first aliquot of the host cells with fatty acid substrate of said protein and with an agent being tested as an inhibitor of said protein;
- 5 (c) culturing a second aliquot of the host cells with fatty acid substrate of said protein;
- (d) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells;
- wherein less uptake of the fatty acid substrate in the first aliquot compared to
- 10 the second aliquot is indicative that the agent is an inhibitor of said protein.
117. The method of Claim 116 further comprising the steps of:
- a) administering the agent to one or more test animals;
- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
- 15 c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
- d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.
- 20 118. A method for identifying an agent which is an inhibitor of a protein, said protein being encoded by (i) a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP2, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:48 under high
- 25 stringency conditions, or by (ii) a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide

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consisting of the amino acid sequence of FATP4, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:52 under high stringency conditions, comprising the steps of:

- 5 (a) introducing into host cells one or more vectors comprising a polynucleotide expressing said protein;
- (b) culturing a first aliquot of the host cells with fatty acid substrate of said protein and with an agent being tested as an inhibitor of said protein;
- (c) culturing a second aliquot of the host cells with fatty acid substrate of said protein;
- 10 (d) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells;

wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of said protein.

119. The method of Claim 118 further comprising the steps of:

- 15 a) administering the agent to one or more test animals;
 - b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
 - c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
 - 20 d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

120. A method for identifying an agent which is an inhibitor of a protein, said protein being encoded by (i) a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid
25 sequence similarity with the amino acid sequence in SEQ ID NO:49 or by (ii) a

nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:53, comprising the steps of:

- 5 (a) introducing into host cells one or more vectors comprising a polynucleotide expressing said protein;
 - (b) culturing a first aliquot of the host cells with fatty acid substrate of said protein and with an agent being tested as an inhibitor of said protein;
 - (c) culturing a second aliquot of the host cells with fatty acid substrate of said protein;
 - 10 (d) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells;
- wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of said protein.

121. The method of Claim 120 further comprising the steps of:

- 15 a) administering the agent to one or more test animals;
- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
- 20 d) comparing the fatty acids of b) with the fatty acids of c).

whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

122. A method for identifying an agent which binds to a protein comprising an amino acid sequence of SEQ ID NO:57, comprising the steps of contacting the agent
25 with the isolated protein under conditions appropriate for binding of the agent to the isolated protein, and detecting a resulting agent-protein complex.

123. The method of Claim 122 wherein the step of contacting the agent with isolated protein is performed in an artificial membrane system.
124. The method of Claim 122 wherein the isolated protein is in isolated plasma membrane.
- 5 125. A method for identifying an agent which inhibits interaction between an isolated protein comprising an amino acid sequence of SEQ ID NO:57, and further comprising a ligand of said protein, comprising:
- (a) combining:
- 10 (1) said isolated protein;
- (2) the ligand of said protein; and
- (3) a candidate agent to be assessed for its ability to inhibit interaction between said protein of (1) and the ligand of (2), under conditions appropriate for interaction between the said protein of (1) and the ligand of (2);
- 15 (b) determining the extent to which said protein of (1) and the ligand of (2) interact; and
- (c) comparing the extent determined in (b) with the extent to which interaction of said protein of (1) and the ligand of (2) occurs in the absence of the candidate agent to be assessed and under the same
- 20 conditions appropriate for interaction of said protein of (1) with the ligand of (2);
- wherein if the extent to which interaction of said protein of (1) and the ligand of (2) occurs is less in the presence of the candidate agent than in the absence of the candidate agent, the candidate agent is an agent which inhibits interaction
- 25 between said protein and the ligand of said protein.

126. The method of Claim 125 wherein (a) is performed in an artificial membrane system.
127. The method of Claim 125 wherein said isolated protein is in isolated plasma membrane.
- 5 128. A method for identifying an agent which binds to a protein, said protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP6, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:56 under high stringency conditions, comprising the steps of isolating the protein, contacting the agent with the
10 isolated protein under conditions appropriate for binding of the agent to the isolated protein, and detecting a resulting agent-protein complex.
129. The method of Claim 128 wherein the step of contacting the agent with the isolated protein is performed in an artificial membrane system.
- 15 130. The method of Claim 128 wherein the isolated protein is in isolated plasma membrane.
131. A method for identifying an agent which inhibits interaction between (1) an isolated protein, said protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP6, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of
20 SEQ ID NO:56 under high stringency conditions, and (2) a ligand of said protein, comprising:

- (a) combining:
- (1) said isolated protein;
 - (2) the ligand of said protein; and
 - (3) a candidate agent to be assessed for its ability to inhibit
- 5 interaction between said protein of (1) and the ligand of (2),
under conditions appropriate for interaction between said protein
of (1) and the ligand of (2);
- (b) determining the extent to which said protein of (1) and the ligand of (2)
interact; and
- 10 (c) comparing the extent determined in (b) with the extent to which
interaction of said protein of (1) and the ligand of (2) occurs in the
absence of the candidate agent to be assessed and under the same
conditions appropriate for interaction of said protein of (1) with the
ligand of (2);
- 15 wherein if the extent to which interaction of said protein of (1) and the ligand of
(2) occurs is less in the presence of the candidate agent than in the absence of the
candidate agent, the candidate agent is an agent which inhibits interaction
between said protein and the ligand of said protein.
132. The method of Claim 131 wherein (a) is performed in an artificial membrane
20 system.
133. The method of Claim 131 wherein the isolated protein is in isolated plasma
membrane.
134. A method for identifying an agent which binds to a protein encoded by a nucleic
acid encoding a fatty acid transport protein consisting of an amino acid sequence
25 sharing at least about 95% amino acid sequence similarity with the amino acid

sequence in SEQ ID NO:57 comprising the steps of isolating the protein, contacting the agent with the isolated protein under conditions appropriate for binding of the agent to the isolated protein, and detecting a resulting agent-protein complex.

- 5 135. The method of Claim 134 wherein the step of contacting the agent with isolated protein is performed in an artificial membrane system.
136. The method of Claim 134 wherein the isolated protein is in isolated plasma membrane.
- 10 137. A method for identifying an agent which inhibits interaction between an isolated protein encoded by a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 90% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:57 and a ligand of said protein, said method comprising:
- 15 (a) combining:
- (1) said isolated protein;
- (2) the ligand of said protein; and
- (3) a candidate agent to be assessed for its ability to inhibit interaction between said protein of (1) and the ligand of (2), under conditions appropriate for interaction between the said protein of (1) and the ligand of (2);
- 20 (b) determining the extent to which said protein of (1) and the ligand of (2) interact; and
- (c) comparing the extent determined in (b) with the extent to which interaction of said protein of (1) and the ligand of (2) occurs in the absence of the candidate agent to be assessed and under the same
- 25

conditions appropriate for interaction of said protein of (1) with the
ligand of (2);

wherein if the extent to which interaction of said protein of (1) and the ligand of
(2) occurs is less in the presence of the candidate agent than in the absence of the
candidate agent, the candidate agent is an agent which inhibits interaction
between said protein and the ligand of said protein.

138. The method of Claim 137 wherein (a) is performed in an artificial membrane
system.

139. The method of Claim 137 wherein said isolated protein is in isolated plasma
membrane.

140. A method for identifying an agent which is an inhibitor of fatty acid uptake by a
protein encoded by a polynucleotide comprising a nucleotide sequence which
encodes a protein consisting of the amino acid sequence in SEQ ID NO:57,
comprising the steps of:

- a) maintaining test cells expressing said polynucleotide in the presence of a
fatty acid and an agent to be tested as an inhibitor of fatty acid uptake;
- b) measuring uptake of the fatty acid in the test cells; and
- c) comparing uptake of the fatty acid in the test cells with uptake of the
fatty acid in suitable control cells;

wherein lower uptake of the fatty acid in the test cells compared to uptake of the
fatty acid in the control cells is indicative that the agent is an inhibitor of fatty
acid uptake by said protein.

141. An inhibitor of fatty acid uptake identified by the method of Claim 140.

142. The method of Claim 140 further comprising the steps of:
- a) administering the agent to one or more test animals;
 - b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from said test animals;
 - 5 c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals;
 - d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.
- 10 143. An inhibitor of fatty acid uptake identified by the method of Claim 142.
144. A method for identifying an agent which is an inhibitor of fatty acid uptake by a protein, said protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP6, wherein said polynucleotide
- 15 hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:56 under high stringency conditions, comprising the steps of:
- a) maintaining test cells expressing said polynucleotide in the presence of a fatty acid and an agent to be tested as an inhibitor of fatty acid uptake;
 - b) measuring uptake of the fatty acid in the test cells; and
 - 20 c) comparing uptake of the fatty acid in the test cells with uptake of the fatty acid in suitable control cells;
- wherein lower uptake of the fatty acid in the test cells compared to uptake of the fatty acid in the control cells is indicative that the agent is an inhibitor of fatty acid uptake by said protein.
- 25 145. An inhibitor of fatty acid uptake identified by the method of Claim 144.

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146. The method of Claim 144 further comprising the steps of:
- a) administering the agent to one or more test animals;
 - b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from said test animals;
 - 5 c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals;
 - d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.
- 10 147. An inhibitor of fatty acid uptake identified by the method of Claim 146.
148. A method for identifying an agent which is an inhibitor of fatty acid uptake by a protein, said protein being encoded by a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:57,
- 15 comprising the steps of:
- a) maintaining test cells expressing said polynucleotide in the presence of a fatty acid and an agent to be tested as an inhibitor of fatty acid uptake;
 - b) measuring uptake of the fatty acid in the test cells; and
 - c) comparing uptake of the fatty acid in the test cells with uptake of the
- 20 fatty acid in suitable control cells;
- wherein lower uptake of the fatty acid in the test cells compared to uptake of the fatty acid in the control cells is indicative that the agent is an inhibitor of fatty acid uptake by said protein.
149. An inhibitor of fatty acid uptake identified by the method of Claim 148.

150. The method of Claim 148 further comprising the steps of:
- a) administering the agent to one or more test animals;
 - b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from said test animals;
 - 5 c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals;
 - d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.
- 10 151. An inhibitor of fatty acid uptake identified by the method of Claim 150.
152. A method for identifying an agent which is an inhibitor of a protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a protein comprising the amino acid sequence in SEQ ID NO:57, comprising the steps of:
- 15 (a) introducing into host cells one or more vectors comprising a polynucleotide expressing said protein;
 - (b) culturing a first aliquot of the host cells with fatty acid substrate of said protein and with an agent being tested as an inhibitor of said protein;
 - (c) culturing a second aliquot of the host cells with fatty acid substrate of said protein;
 - 20 (d) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells;
- wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of said protein.
153. The method of Claim 152 further comprising the steps of:
- 25 a) administering the agent to one or more test animals;

- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
- 5 d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

154. A method for identifying an agent which is an inhibitor of a protein, said protein being encoded by a polynucleotide comprising a nucleotide sequence which
- 10 encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP6, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:56 under high stringency conditions, comprising the steps of:
- (a) introducing into host cells one or more vectors comprising a
- 15 polynucleotide expressing said protein;
- (b) culturing a first aliquot of the host cells with fatty acid substrate of said protein and with an agent being tested as an inhibitor of said protein;
- (c) culturing a second aliquot of the host cells with fatty acid substrate of said protein;
- 20 (d) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells;
- wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of said protein.

155. The method of Claim 154 further comprising the steps of:
- 25 a) administering the agent to one or more test animals;

- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
- 5 d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

156. A method for identifying an agent which is an inhibitor of a protein, said protein being encoded by a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:57, comprising the steps of:

- (a) introducing into host cells one or more vectors comprising a polynucleotide expressing said protein;
- 15 (b) culturing a first aliquot of the host cells with fatty acid substrate of said protein and with an agent being tested as an inhibitor of said protein;
- (c) culturing a second aliquot of the host cells with fatty acid substrate of said protein;
- (d) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells;
- 20 wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of said protein.

157. The method of Claim 156 further comprising the steps of:

- a) administering the agent to one or more test animals;
- 25 b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;

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- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
- d) comparing the fatty acids of b) with the fatty acids of c).

whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

5

158. A method for identifying an agent which is an inhibitor of a fatty acid transport protein, comprising the steps of:

10

- (a) introducing into cells one or more vectors comprising a gene encoding a cell surface protein and a nucleic acid encoding the fatty acid transport protein;
- (b) contacting the host cells with anti-cell surface protein antibody and labeled fatty acid substrate of the fatty acid transport protein;
- (c) contacting a first aliquot of the host cells with an agent being tested as an inhibitor of the fatty acid transport protein, while leaving a second aliquot of the host cells uncontacted with the agent;
- (d) identifying, in the first and second aliquots, the host cells expressing the cell surface protein by detecting the anti-cell surface protein antibody bound to the host cells; and
- (e) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells identified as expressing the cell surface protein;

15

20

wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of the fatty acid transport protein.

25 159. The method of Claim 158 wherein the host cells regulably express the FATP4 gene.

160. The method of Claim 158 wherein the host cells are prokaryotes.
161. The method of Claim 158 wherein the prokaryotes are *E. coli*.
162. The method of Claim 158 wherein the fatty acid is a radioactively labeled fatty acid.
- 5 163. A method for identifying an agent which is an inhibitor of FATP4, comprising the steps of:
- (a) introducing into cells one or more vectors comprising a gene encoding a cell surface protein and a nucleic acid encoding FATP4;
 - 10 (b) contacting the host cells with anti-cell surface protein antibody and labeled fatty acid substrate of FATP4;
 - (c) contacting a first aliquot of the host cells with an agent being tested as an inhibitor of FATP4, while leaving a second aliquot of the host cells uncontacted with the agent;
 - 15 (d) identifying, in the first and second aliquots, the host cells expressing the cell surface protein by detecting the anti-cell surface protein antibody bound to the host cells; and
 - (e) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells identified as expressing the cell surface protein;
 - 20 wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of FATP4.
164. The method of Claim 163 further comprising the steps of:
- a) administering the agent to one or more test animals;

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- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
- 5 d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

165. The method of Claim 163 wherein the cell surface protein is CD2.

166. The method of Claim 163 wherein the fatty acid substrate is BODIPY-labeled.

- 10 167. A method for detecting, in a sample of cells, a nucleic acid molecule comprising at least about 90% sequence similarity to SEQ ID NO:48, comprising:
- a) purifying nucleic acid from the cells;
- b) hybridizing 1) purified nucleic acid from the cells to 2) purified nucleic acid comprising SEQ ID NO:48, under conditions that allow
- 15 hybridization between 1) and 2) if the sequences of 1) and 2) have at least about 90% sequence similarity; and
- c) detecting resulting hybrid nucleic acids in the hybridization; wherein, if hybrid nucleic acids are detected at a significant level compared to a suitable control hybridization, then a nucleic acid molecule comprising at
- 20 least about 90% sequence similarity to SEQ ID NO:48, has been detected.

168. A method for detecting, in a sample of purified nucleic acid, a nucleic acid molecule having at least about 90% sequence similarity to SEQ ID NO:48, comprising:

- a) hybridizing 1) the sample of purified nucleic acid to 2) purified nucleic acid comprising SEQ ID NO:48, under conditions that allow hybridization between 1) and 2) if the sequences of 1) and 2) have at least about 90% sequence similarity; and
- 5 b) detecting resulting hybrid nucleic acids in the hybridization; wherein, if hybrid nucleic acids are detected at a significant level compared to a suitable control hybridization, then a nucleic acid molecule comprising at least about 90% sequence similarity to SEQ ID NO:48, has been detected.
- 10 169. A method for identifying (1) nucleic acid molecules in fixed cells which specifically interact with a (2) nucleic acid molecule comprising the nucleotide sequence in SEQ ID NO:48, said method comprising the steps of:
- a) adding to the fixed cells the nucleic acid molecule comprising a nucleotide sequence in SEQ ID NO:48;
- 15 b) incubating the fixed cells under conditions allowing hybridization of (1) with (2);
- c) removing the nucleic acid molecule of step a) that has not hybridized; and
- d) detecting hybrid molecules comprising (1) and (2).
- 20 170. A method for detecting FATP2 in a sample of cells, comprising the steps of adding an agent that specifically binds to FATP2 to the sample, and detecting agent specifically bound to the FATP2.
171. The method of Claim 170 wherein the agent is an antibody which binds to FATP2.

172. A method for detecting FATP2 in a sample of cell lysate, comprising the steps of adding an agent that specifically binds to FATP2 to the sample, and detecting agent specifically bound to the FATP2.
173. The method of Claim 172 wherein the agent is an antibody which binds to
5 FATP2.
174. An isolated antibody which binds to a polypeptide having an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:49.
175. An isolated antibody which binds to a fatty acid transport protein having the
10 amino acid sequence in SEQ ID NO:49.
176. A method for detecting, in a sample of cells, a nucleic acid molecule comprising at least about 90% sequence similarity to SEQ ID NO:52, comprising:
- a) purifying nucleic acid from the cells;
 - b) hybridizing 1) purified nucleic acid from the cells to 2) purified nucleic
15 acid comprising SEQ ID NO:52, under conditions that allow hybridization between 1) and 2) if the sequences of 1) and 2) have at least about 90% sequence similarity; and
 - c) detecting resulting hybrid nucleic acids in the hybridization; wherein, if
20 hybrid nucleic acids are detected at a significant level compared to a suitable control hybridization, then a nucleic acid molecule having at least about 90% sequence similarity to SEQ ID NO:52, has been detected.

177. A method for detecting, in a sample of purified nucleic acid, a nucleic acid molecule comprising at least about 90% sequence similarity to SEQ ID NO:52, comprising:
- 5 a) hybridizing 1) the sample of purified nucleic acid to 2) purified nucleic acid comprising SEQ ID NO:52, under conditions that allow hybridization between 1) and 2) if the sequences of 1) and 2) have at least about 90% sequence similarity; and
- 10 b) detecting resulting hybrid nucleic acids in the hybridization; wherein, if hybrid nucleic acids are detected at a significant level compared to a suitable control hybridization, then a nucleic acid molecule having at least about 90% sequence similarity to SEQ ID NO:52, has been detected.
178. A method for identifying (1) nucleic acid molecules in fixed cells which specifically interact with a (2) nucleic acid molecule comprising the nucleotide sequence in SEQ ID NO:52, said method comprising the steps of:
- 15 a) adding to the fixed cells the (2) nucleic acid molecule comprising a nucleotide sequence in SEQ ID NO:52;
- b) incubating the fixed cells under conditions allowing hybridization of (1) with (2);
- 20 c) removing the nucleic acid molecule of step a) that has not hybridized; and
- d) detecting hybrid molecules comprising (1) and (2).
179. A method for detecting FATP4 in a sample of cells, comprising the steps of adding an agent that specifically binds to FATP4 to the sample, and detecting agent specifically bound to the FATP4.
- 25

180. The method of Claim 179 wherein the agent is an antibody which binds to FATP4.
181. A method for detecting FATP4 in a sample of cell lysate, comprising the steps of adding an agent that specifically binds to FATP4 to the sample, and detecting agent specifically bound to the FATP4.
182. The method of Claim 181 wherein the agent is an antibody which binds to FATP4.
183. An isolated antibody which binds to a polypeptide having an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:53.
184. An isolated antibody which binds to a fatty acid transport protein having the amino acid sequence in SEQ ID NO:53.
185. A method for detecting, in a sample of cells, a nucleic acid molecule comprising at least about 90% sequence similarity to SEQ ID NO:56, comprising:
- a) purifying nucleic acid from the cells;
 - b) hybridizing 1) purified nucleic acid from the cells to 2) purified nucleic acid comprising SEQ ID NO:56, under conditions that allow hybridization between 1) and 2) if the sequences of 1) and 2) have at least about 90% sequence similarity; and
 - c) detecting resulting hybrid nucleic acids in the hybridization; wherein, if hybrid nucleic acids are detected at a significant level compared to a suitable control hybridization, then a nucleic acid molecule having at

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least about 90% sequence similarity to SEQ ID NO:56, has been detected.

186. A method for detecting, in a sample of purified nucleic acid, a nucleic acid molecule comprising at least about 90% sequence similarity to SEQ ID NO:56, comprising:
- 5
- a) hybridizing 1) the sample of purified nucleic acid to 2) purified nucleic acid comprising SEQ ID NO:56 under conditions that allow hybridization between 1) and 2) if the sequences of 1) and 2) have at least about 90% sequence similarity; and
 - 10 b) detecting resulting hybrid nucleic acids in the hybridization; wherein, if hybrid nucleic acids are detected at a significant level compared to a suitable control hybridization, then a nucleic acid molecule comprising at least about 90% sequence similarity to SEQ ID NO:56 has been detected.
187. A method for identifying (1) nucleic acid molecules in fixed cells which specifically interact with a (2) nucleic acid molecule having the nucleotide sequence in SEQ ID NO:56, said method comprising the steps of:
- 15
- a) adding to the fixed cells the (2) nucleic acid molecule comprising the nucleotide sequence in SEQ ID NO:56;
 - b) incubating the fixed cells under conditions allowing hybridization of (1) with (2);
 - 20 c) removing the nucleic acid molecule of step a) that has not hybridized; and
 - d) detecting hybrid molecules comprising (1) and (2).

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188. A method for detecting FATP6 in a sample of cells, comprising the steps of adding an agent that specifically binds to FATP6 to the sample, and detecting agent specifically bound to the FATP6.
189. The method of Claim 188 wherein the agent is an antibody which binds to
5 FATP6.
190. A method for detecting FATP6 in a sample of cell lysate, comprising the steps of adding an agent that specifically binds to FATP6 to the sample, and detecting agent specifically bound to the FATP6.
191. The method of Claim 190 wherein the agent is an antibody which binds to
10 FATP6.
192. An isolated antibody which binds to a polypeptide having an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:57.
193. An isolated antibody which binds to a fatty acid transport protein having the
15 amino acid sequence in SEQ ID NO:57.
194. A method for modulating fatty acid uptake of cells in culture, comprising adding one or more agents that modulate fatty acid uptake to cells comprising one or more fatty acid transport proteins.
195. The method of Claim 194 wherein the agent modulates fatty acid uptake by
20 modulating biosynthesis of one or more fatty acid transport proteins.

196. The method of Claim 195 wherein the agent modulates fatty acid uptake by modulating biosynthesis of FATP6.
197. The method of Claim 196 wherein the agent is an antisense oligonucleotide.
198. A method for inhibiting fatty acid uptake in the small intestine of a mammal,
5 comprising administering to the mammal a therapeutically effective amount of an agent which is an inhibitor of fatty acid uptake by a fatty acid transport protein in the small intestine of the mammal.
199. The method of Claim 198 wherein the agent is administered orally.
200. The method of Claim 198 wherein the fatty acid transport protein is hsFATP6.
- 10 201. A method for inhibiting fatty acid uptake in cardiac muscle of a human comprising administering to the human a therapeutically effective amount of an agent which is an inhibitor of fatty acid uptake by FATP6.
202. A method for directing an agent to cardiac muscle in a mammal, comprising
15 administering to the mammal a complex which comprises the substance and a moiety which binds to FATP6.
203. A method for directing an agent to liver in a mammal, comprising administering to the mammal a complex which comprises the substance and a moiety which binds to FATP5.

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204. A method for detecting a variant allele of a human FATP gene, comprising:
- a) preparing amplified, purified reference DNA encoding all or a portion of a FATP from a human, and amplified, purified test DNA encoding all or a portion of the FATP from a human to be tested as having a variant allele;
 - b) determining whether the reference DNA and test DNA differ in DNA sequence;
- wherein, if the test DNA differs in sequence from the reference DNA, the test DNA comprises a variant allele of a human FATP gene.

mmFATP1
mmFATP2
mmFATP3
mmFATP4
mmFATP5
ceFATP8
scFATP
miFATP

64
41
35
1
74
63
64
35

mmFATP1
mmFATP2
mmFATP3
mmFATP4
mmFATP5
ceFATP8
scFATP
miFATP

126
101
9
8
140
125
134
54

mmFATP1
mmFATP2
mmFATP3
mmFATP4
mmFATP5
ceFATP8
scFATP
miFATP

195
171
164
56
213
154
204
164

mmFATP1
mmFATP2
mmFATP3
mmFATP4
mmFATP5
ceFATP8
scFATP
miFATP

265
241
234
125
283
264
273
223

mmFATP1
mmFATP2
mmFATP3
mmFATP4
mmFATP5
ceFATP8
scFATP
miFATP

336
311
304
196
353
335
344
295

mmFATP1
mmFATP2
mmFATP3
mmFATP4
mmFATP5
ceFATP8
scFATP
miFATP

406
381
374
266
423
404
417
365

mmFATP1
mmFATP2
mmFATP3
mmFATP4
mmFATP5
ceFATP8
scFATP
miFATP

473
446
439
333
488
473
489
423

mmFATP1
mmFATP2
mmFATP3
mmFATP4
mmFATP5
ceFATP8
scFATP
miFATP

544
517
510
404
559
544
562
494

mmFATP1
mmFATP2
mmFATP3
mmFATP4
mmFATP5
ceFATP8
scFATP
miFATP

611
585
578
471
627
616
562

Figure 1

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Fig. 2A

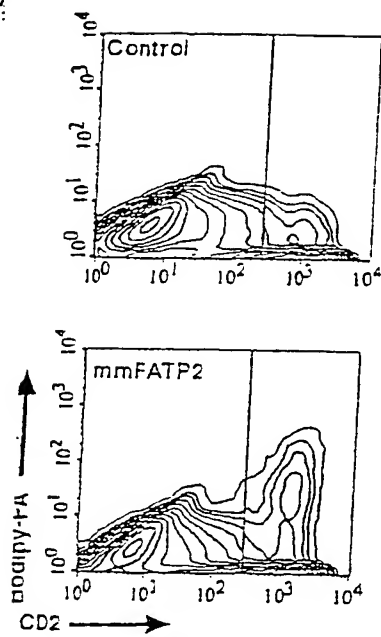


Fig. 2C

Fig. 2B

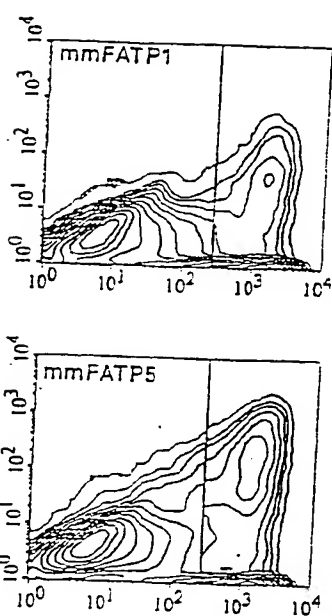


Fig. 2D

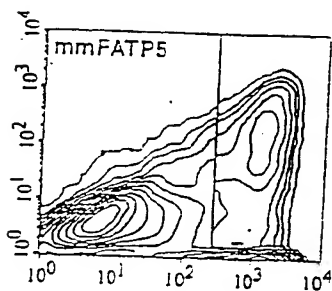


Fig. 3

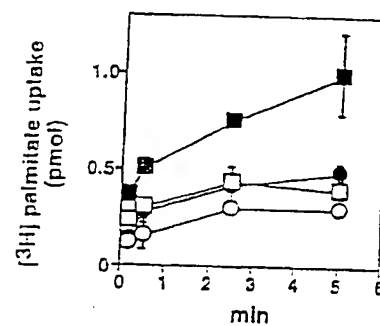
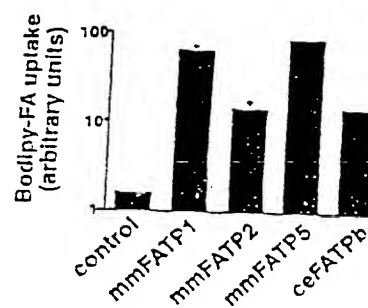


Fig. 4

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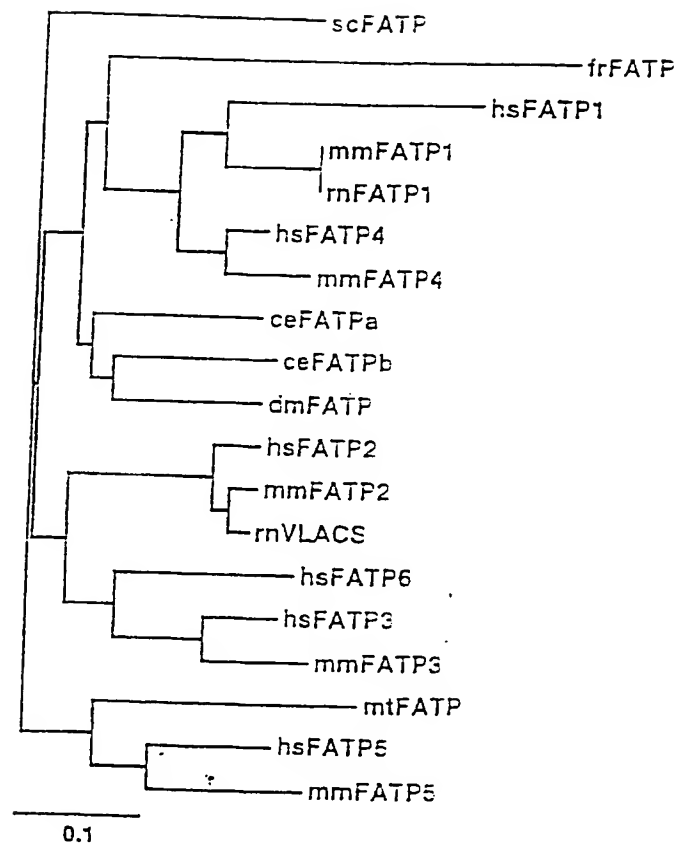


Figure 5

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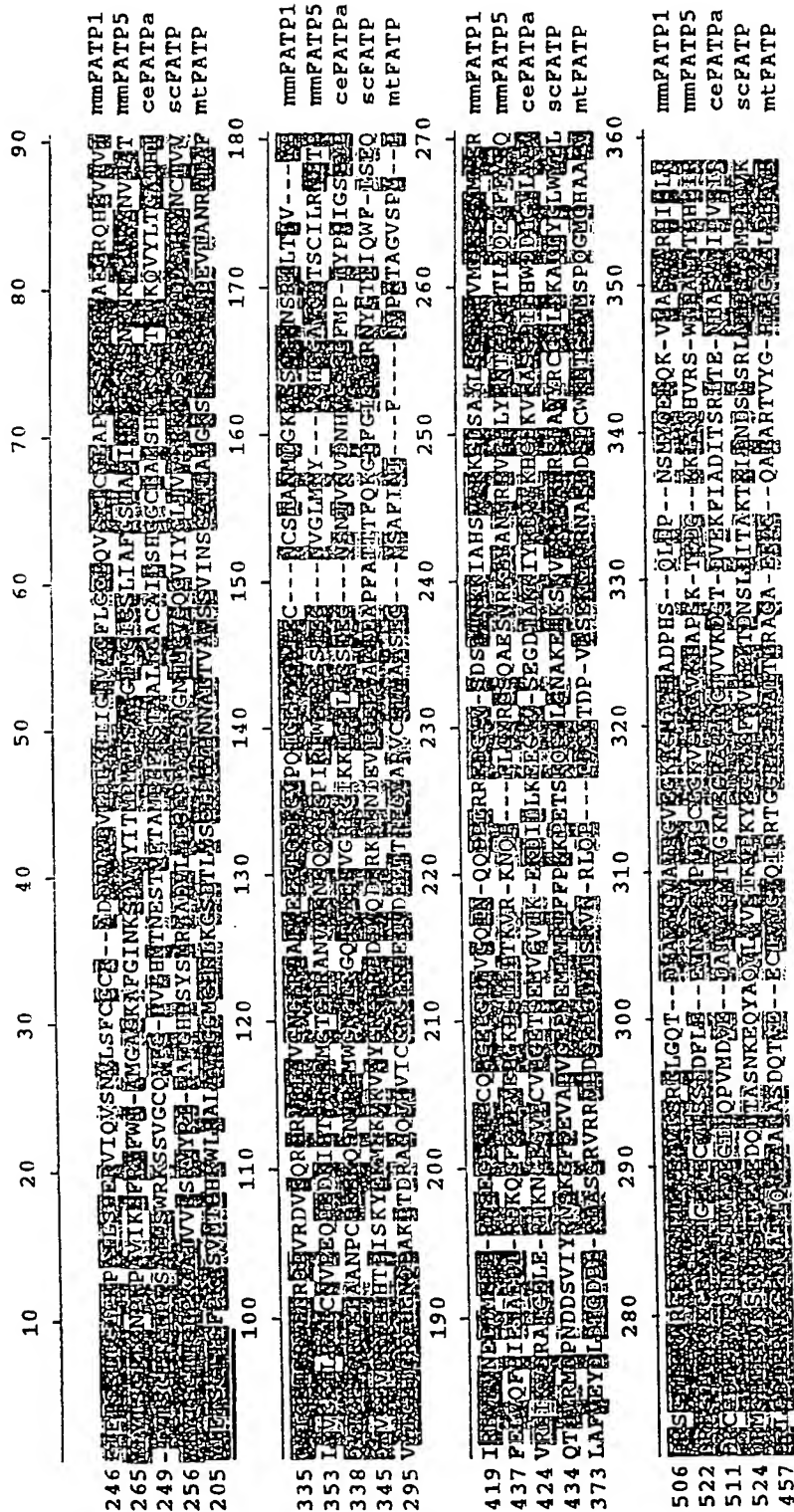


Figure 6

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[illegible]

Figure 7

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mmFATP3 DNA sequence

AACACTCACTATAGGGTCAAGGTATGAGTGGCATGCCAC 40
GGGTAAAGCTTGGGCCCCCTCGAGGCTTCTCTATAGGGGCC 80
GGCGAAGGCGAAGGCTCTGATAGGGGCTGAGTCTGGGCT 120
GGGCTCTGCGGTAACTGGCCCCGGGAGGAGGCGACACATAC 160
CTTCTCTATCGAAGGGGGGCGAGGCTTTAGCTAAGGGGAG 200
GCTGAGGGGGAGAGGCAAGGGATTGCTGGGGCTTTCTGC 240
GGGTAAGGGGGCTGCAAGGGGGGCTGCGAGGCTGGGGGAG 280
GGGTAGCACTGAGGAAGGGGCAAGGGTGGGGCTTGGGCT 320
GGAGATGGGGCTGCTATAGGGGAGCAAGGGGCCCCCTCTGG 360
CAACCGGGGGGCAAGGTGGGGCTGCTCTCTCCAGGGGGCC 400

Figure 8A

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GCATTTTCCTTTGGATTTCGTTGGCACTGGCCAAAGCTGGC 440
CTGGGCAAGGCTTTTGTGCCCAGGCTTTTACGGCCAGGAC 480
CCCTGCTGCACTGCTCCGGAGCTGGGGTGGGAGTGGCT 520
CGTGCTGGCCACAGATTTCCTGGAGTCCCTGGAGCGGAC 560
CTGGCGGCTTTCAGGCAATGGGGCTCCACCTATGGGGCA 600
CGGGCCCTCAACTAATGTAGCTGCAATCAGCAATTTGCT 640
ATCGGAGGAGGACCAAGTGGATCAGGCAAGTGGGGG 680
TACCTCTCTGCCCCCAACATAATGCAACCTGGCTGT 720
ACATCTTCACTCTGTGGTACTAGGGCTGGCCAGGCTGC 760
TCCATTCAGTCTCTAGGTTCTACAGTGGCAAGGATTTC 800
TACCATCTGTGTGGTGGTCCAGGAGGAGGCTCTTACC 840
TOGCACTCCCACTGTACCATGTCTGGCTCCCTTCTGG 880
CATTTGTGGGTGCTTGGGCAATGGGGCAAGGTTGGTGT 920
AAACCCAGGTTCTCAGCTAGGCAAGTCTGGGCAAGTTGG 960
AGAAACACAGGGTCAAGTCTGGTCCAGTATGGGGAGTT 1000
GTGGGATACCTGTCAACAGTCCCGGCAAGGCAAG 1040
TTTGACCATAGGTTGGGTTGGGAGTGGGCAAGGTTGG 1080
GCCCACACACTGGGAGGCTTCTGGGGCAATTTGGTACC 1120
TCTGCACTACTGGTCAAGTATGGCATGACAGGGCAAC 1160
GTAGCTACGTTCAATTACACAGGAGGGAGGGTGGAGTGG 1200
GGGAGCTTCTGGCTTTTACAGCAATCTTCCGCTTCTC 1240
CTTGATTCCATAGGTTGTATGACAGGGGAGGCTATTGG 1280
AATGCCCAGGGGCACTGGTATGACCAATCTCCAGGTGAGC 1320
CAGGCTACTGGTGGGCGGAGTGGGAGGAGTCCGCTT 1360
CCTGGGCTATGCTGGGGCTCCGAGGCTGGGCAAGGCAAG 1400
CTGCTCAAGGATGCTCTTCTGGTCTGGGAGGTTTCTCTCA 1440
ATACTGGGCACTCTTGGTCTGTGATGAGCAAGGCTTCT 1480
TCACTTCCAGGATGGTACTGGACACACCATCAGGTGAG 1520
GGACAGATGTGGGCAACTGAGTGGCTGAGGCTCTTGG 1560
AGACCCGGGACTTCCCTCAGGAGGTGAACATCTATGGAGT 1600
CAGGTTGGGAGGGCAAGGAGGGGAGGATGGGGG 1640
TTGGCTCTGGGCGGCGGAGGCTCTCAACTGGTGGAGC 1680
TCTACAGGATGTTTCTGCAACTTGGCAAGGATGGG 1720
AAGTGGGTTCTCAGGCTCAGCAATCTTTGGGCACTACT 1760
GACACCTTCAACAGGAGAGGTTAGGATGGGCAATGAG 1800
GCTTTCAACCCAGTGTACTGTCTCAACCACTCTATGTTCT 1840
GGACCAAGATATAGGGGCTTACCTGGGCTCAGACCTGGC 1880
GGTACAGTGGGCTCTGTCTGAGCACTTCCATCTGAA 1920
AAGTCCACTTCAAGGAGGGGCTGGGAGGTTACAGGCAAC 1960
CATGGCTGCAACAGGAGGGTTTGGGGTATCTTTTGTAT 2000
ATGGAGTCAATTATTTTGTATAAAGAGCTGGAGCTTAAA 2040
AA 2080
AAAAAAA 2087

Figure 8B

mmFATP3 protein sequence

AADPESSESGCSLAWRLAYLAREQPIHTFLIHEAQRFSYAEAERESNRIA 50
 RAFLRARGWIGERRGSGRGSTEECARVAPPAGDAARGITAPPLAPGATV 100
 ALLLPAGEPDFLWIWFGAKAGLRITAFVPTALRRGPLLHCLRSOGASALVL 150
 ATEFLESLEPDLPALRAMEHLWATGPEINWAGISNLLSEAADQVDFVP 200
 GYLSAPQNMIDTCLYFTSGITGLPKAARISHLKVLQQGFYHLCGVHQE 250
 DVTYIALPLYHMSGSLIGIVGCLGIGATVVLKPKFSASQFWDDQKHRVT 300
 VFQYIGELCRYLVNQPPSKAEFDHKVRLAVGSLRPDIWERFLRRFGPLQ 350
 ILHTYGMTEGNWATFNNTGRQGAVERASWLYKHIFPFSLTRYDMTICEPI 400
 RNAQGHOMITSPGEFGLLVAPVSQQSPFLGYAGAPELAKDKLLKIVFWSG 450
 DWFFNTGDLMLVDEQGFHFHFDRTGDTTRWKGENWATTEVAEVLETIDFL 500
 QEVNIYGVIVPGHEGRAGMAALALRPPQALNLVQLYSHVSENLPYARPR 550
 FLRLQESLATTETFKQOKVRMANEGFDPSVLSDFLYVLDQDIGAYLPLTP 600
 ARYSALLSEELRI 613

Figure 9

mmFATP4 DNA sequence

CCCAAGCGTCCGCCCCAAGCGTCCGGCATGGCCAAGCTGGG 40
 CGTGGAGGGGCTCTCATCAACACCAACCTTAGGGGGGAT 80
 GCGCTGGGCACTGTCTTGACAACCTCAAGGCAAGAGCTC 120
 TCATCTTTGGCAGTCAGATGGGCTCAGCTATCTGTGAGAT 160
 CCATGCTAGCCTGGAGGCCACACTCAGGCTCTTCTGCTCT 200
 GGATCCTGGGAGGCCAGCAGAGTGCCCGTCAGCAGAGC 240
 ATCTGGACCTCTTCTGGAAGATGCCCCGAGCAGCTGCC 280
 CAGTCAGCCAGACAAGGGTTTACAGATAAGCTCTTCTAC 320
 ATCTACACATCGGGCAACAGGGGCTAOCCTAAGCTGCCA 360
 TTGTGGGTGCACAGCAGGTATTATCGTATGGCTTCCCTGGT 400
 GTACTATGCTATCCGCTATGGGCTGATGACATTGTCTAT 440
 GACTGCGTCCCCCTCTAOCCTCAAGCAGCAACATCGTG 480
 GGGATTGGCAGTCTTACTCCAGGCTATGACTGTGGTGAT 520
 CCGGAGAGGTTCTCAGGCTCCCGGTTCTGGGATCATGT 560
 ATCAAGTACAACTGCACAGTGGTACAGTACATTGGCGAGC 600
 TCTGCGGCTACCTCTGAACAGCCACCCCGTGAGGCTCA 640
 GTCTGGCCACAAGGTGGGATGGCAGTGGGCAAGGTTCTC 680
 CGGCAGTCCATCTGGAAGGACTTCTCCAGCGTTTCCACA 720
 ...

Figure 10A

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TCCCCCAGGTGGCTCAGTTCTATGGGGCCACTCAATGCAA 760
CTGTAGCCTGGGCAACTTTTCACAGCCGGTGGGGGCTGT 800
GGCTTCAATAGCCGATCCTGTCTTTTGTGTACCCATCC 840
GTTTGGTAAGTGTCAATCAGGATACCATGCAACTGATCCG 880
GGCACCAGATGCACTCTGCAATTCCTGTCAACCAGGTAC 920
CCAGGCCAGCTGGTGGGTGGATCATCCAGCAGGACCTTC 960
TGGGCGGTTCGACGGGTACCTCAACCAAGGTGGCAACA 1000
CAACAACATTTGCTAATGATGTCTTCAAGAGGGGGCAACA 1040
GCTTACCTCACTGGTCACTCTGTGTGATGCAATGCTGG 1080
GTAACTGTACTTCCGATATGGCACTGGGGCACTGTCCG 1120
CTGCAAGGGGCAATGTATCTAACCCTGAGGTGGAGGGC 1160
AACAATCAGCCGCTGCTTCTATGGCACTGTGGCAGTTT 1200
ATGCTGTTCAGGTGGGAGCACTCAAGGCGGCAAGGAT 1240
GGCTGGCGTTGCAAGTCCCATCAGCAACTGTGACCTGGAG 1280
AGCTTTGCACAGACCTTCAAAAAGGAGCTGCTCTGTATG 1320
CCCGCCCATCTTCTGCTGCTTCTTGGCTGAGCTGCACAA 1360
GACAGGGACCTTCAAGTTCAGCAACACACAGTTGGGAAG 1400
GAGGGCTTTGACCCATCTGTGTGCAAGACCCGCTGTCT 1440
ATCTGATGCTCGCAAGGGCTGCTAGGTTCAGCTGCAACA 1480
GAGGGCTATACCCGATCCAGGCAAGGCAAGGCAAGCTG 1520
TGATTTCCCCCTACATCCCTCTGAGGGCCAGAGATGCTG 1560
GATTCAGAGCCCTAGGCTCCACCCCAAGGGTCTCTGGCA 1600
ATGCCAGACCAAGCTAGCAGGGCCCGCACTCCGCCCCCT 1640
AGGTGCTGATCTCCCTCTCCCAAACTGCCAAGTCACTCA 1680
CTGGCGCTTCCCCCACTCCCAAGGCTTTCTGTGAAAGT 1720
CTCATCCAGCTGTGTCTTCTGGTCCAGGGGTGGCCCCCTG 1760
GCCCCAGGTTTCTGATAGGCTCTTTAGGATGGTATCTT 1800
GGGTCCAGCGGGCCAGGGTGTGGGCAAGGAGTCACTAGA 1840
TCCCTCCAATCAGAGGCTAGCTTACAAAGCAACCAAGGCA 1880
AAGCTGTACACTCAGCAAGCTAAGTGGCCAGAGACTATA 1920
GTTGCCAGTATCCCATGTCCACAGAGGATCTTGGTCCAG 1960
AGCTGCCAAAGTGTCACTCTCTCCCTGCTGCACTCTGGG 2000
GAAAAGGCAAGCATGTGGCCACTGGGCACCTGTCTCAA 2040
GAGTCAAGGATCACAACACTCAGTCTTGTCTCTCCAGGT 2080
CCCTGTCTCTGTCTCGGGAGGGAGGGCAAGGTGTCTG 2120
TCTGTCTCTCTGCTGTCTGTGAGTCTGTGTGTCTCTC 2160
CATCTGTCTAGCTCAGTGTGGGTGCAACAGGCATCAGG 2200
AGAGTGTGGCTCAGGGGCCAATAAACTCTGCTTCACTCC 2240
TCTTAAAAA 2280
AAAAA 2301

Figure 10B

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mmFATP4 protein sequence

HASAHASGMAKLGVEAALININLRDALRHCLDTSKARAL 40
 IFGSEMASAICEIHASLEPTLSLFCSGSWEPSTVPVSTEH 80
 LDPLLEDAPFKHLPSPHDKGFTDKLFYTYTSGTTGLEPKAAT 120
 VVHSRYYYRMASLVYYCFMRPDDIVYDCLPLYHSSRKHRG 160
 LWQCLLHEMTVVRKKFSASRFWDDCTKYNCTVVOYIGEL 200
 CRYLLNQPPREAESRHKVRMALGNGLRQSTWIDFSSRFHI 240
 PQVAEFYGFATECNCSLGNFDSRVGACCFNSRILSFVYPIR 280
 LVRVNEIDIMELIRGPDGVCTPQQPGQPGQLVGRITIQDDPL 320
 RRFDDGVLNQGANNNKTIANDVEKKEDQAVLTGDLVMDDELG 360
 VLYFRRTGCTIFRWKGENVSTTEVEGILSRLLHMAADVAVY 400
 GVEVPGETEGRAGMAAVASPISNCHLESFAQITLKKELFLYA 440
 RPIFLRFLPELHKTGIFKFQKTELKKEGFDPSVVKDPLFY 480
 LDARKGCVVALDQEFAYTRIQAGEEKL 507

Figure 11

mmFATP5 DNA sequence

CACTCATCAGAGCTAAGAGACACTACAGGCTCTCATCTAC 40
 TTCAGAAAGAGCCCAATGCCATGGGATATTTGGAAGAACTA 80
 ACCTTACTGCTGTGTGCTGTCTGTCTGCTGGTGGCTGGGGC 120
 AGCCCCCATGGCCAGCAGCTATGGCTCTGGCCCTGGCGTTG 160
 GTTCTCTGGGAGACCCACATGCCCTGTGTCTGTCTGGCTTG 200
 GCATTGCTGGGCAGACCCCTGGATCAGCTCCTGGATGCCCC 240
 ACTGGCTGAGCCTGGTAGGAGCAGCTCCTTACCTTATTCT 280
 ATTGCCCTCTACAGCCACCCCCAGGGCTACGCTGGCTGCAT 320
 AAAGATGTGGCTTTCACTTCAAGATGCTTTTCTATGGCC 360
 TAAAGTTTCAAGGCAAGCCTTAACAAACATCCTCCAGAGAC 400
 CTTTGTGGATGCTTTAGAGGGCAAGCACTGGCATGGCCT 440
 GACCGGGTGGCCTTGGTGTGTACTGGGTCTGAGGGCTCT 480
 CATTCAAAATAGCCAGCTGCTGATGOCAGGTCTGTGAGGC 520
 AGCATGGGTCTGAAAGCAAAGCTGAGGATGCGGTAAATC 560
 CAGACACAAGAGATGCTGTCTGTATCTTAGTTCTCTCCCT 600
 CCAAGGACCATTTCTGCTTTTCACTGTGTCTCTGGGGTGGC 640
 CAAGTTGGGCTGGCCTGTGGCTGCTATCAATCCACACAGC 680
 CGAGGGATGGCCCTTGGCTACACTCTGTACCGAGCTCTGGGG 720
 CCAGTGTGCTGATTGTGGATCCAGAACTCCAGCAACCT 760
 GGAAGAGTCTCTCCCAAGCTGCTAGCTGACAAACATTAC 800

Figure 12A

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TGCCTTCACCTTGGCCACAGCTCACCCACCCCGGAGTAG 840
 AGGCTCTGGGAGCTTCCCTGATGCTGCTACTTCTGACCC 880
 ACTACCTGGCAGCCTTCAGCTACCTTTAAGTGGAAATCT 920
 CCTGGCATATTTCATCTTTACTTTCAGGACCCACTGGACTCC 960
 CAAAGCCAGCCATCTTTATCAGATGAGGGGTCATACAGT 1000
 CAGCAACGTCCTCTCTCTCTCTGCTGCTGCTGCTGCTGCT 1040
 GGGCTCTATCAGCTCTACCTCTCTGCTGCTGCTGCTGCTGCT 1080
 TTTCTCTTGGATCTCTCTGCTGCTGCTGCTGCTGCTGCTGCT 1120
 CTCTCTCTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1160
 GCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1200
 TGGCTCAATCTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1240
 ACCAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCA 1280
 ACTGCTCTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1320
 GCTTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1360
 AGAGGGCAATGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1400
 GGGCTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1440
 CTCTCTCTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1480
 GCTCTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1520
 CCAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCA 1560
 ACCAAGCTCTCTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1600
 CAATGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1640
 CIGTACTTCAAGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1680
 AAGGCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCT 1720
 CCGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1760
 TGTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCT 1800
 TCTATGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1840
 CATGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1880
 GGGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAG 1920
 CCTATGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1960
 GCAATCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCT 2000
 GTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 2040
 TCTACATACTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 2080
 CATGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 2120
 AATCT 2160
 TGTACAGCTTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCT 2200
 GTTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 2240
 CTTCAATCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 2277

Figure 12B

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mmFATP5 protein sequence

MALALRWFLGDPICLVILGLALIGRFLWSSWMFHWLSLVG 40
AAILTLFLILPLQPPFGLRWLHKDVAFTFKMLFYGLKFRRL 80
NKHPPETFDALERQALAWPDRVALVCTGSEGSSTINSQL 120
DARSCQAAWLWKAKLKDAVIQNRDAAAILVLPSTTISAL 160
SVFLGLAKLGCPVAWINPHSRGMPLIHSVRSSGASVLIVD 200
PDLOENLEEVLPKLLAENIHCFYLGHSSPTPGVEALGASL 240
DAAPSDFPVASLRATIKWKSPAIFIFTSGTTGLEKPAILS 280
HERVIQVSNVLSFCGCRADDWYDVLPLYHTTGLVLGFLG 320
CLQMGATCVLAPKFSASRFWAECRQHGIVIVILYVETILRY 360
LQWPEQPEDKIHIVRLAMETGLRANWKNFQORFGPTRI 400
WEFYGSTEGWGLMNYVGHGAVERTSCILRLITPFFELWQ 440
FDIETAEPLRDKQGFCLPVERGKFGILLIKVRKNQPFILGY 480
RGSQAESNRKLVANVRRVEDLYFNTEGVLITLDQEGFFYFQ 520
IRLGDTFRWKGENVSTIGEVECVLSSLDLEEMNVYGVVPV 560
GTEGKVGMAAVKLAPKQTFDGGKLYQHVRSLPAYATPHF 600
IRIQDSLETTNTYKLVKSRLVREGFTVGLIADPLYILINK 640
AQIFRSIMFDVYQAVCEGIWNL 663

Figure 13

hsFATP2 DNA sequence

ATGGGATTGACTCTTTCTGACAAAGTGCATGAAGTATC 40
AACTGAACCTATCCCAGAGTCATGGAGGCTGGAAGTCACT 80
TTTTCACATCCTGCGTTATACATTTATACITCTGGAACCA 120
CAGGCTCTTCCAAAAGCAGGCATGATCACTCATCAGCGCAT 160
ATGGTATGGCACTGGGCTCACTTTTGTAGGGATTGAAG 200
GCAGATGATGTCATCTATATCACTCTGCGCTTTTACCACA 240
GTGCTGCACTACTGATTGGCATTCAGGATGATTTGTGGC 280
TGGTGCTACTCTTGCGTTGCGGCTAAATTTTCAGGCAGC 320
CAGTTTGGGATGACTGCAGAAAATACAAAGTCACTGICA 360
TTCAGTATATCGGTGAAGTCTTGGTATTTATGCAACTC 400
ACCACAGAAACCAATGAACGTGATCATAAAGTGACACTG 440
GCACTGGGAAATGGCTTACGAGGAGATGIGTGGACACAAT 480
TTGTCAAGAGATTTGGGACATATGCACTCTATCAGTTCTA 520
TGCTGGCACTGAAGCAATATTTGGATTTATGAATTATGCG 560
AGAAAAGTTGGTCTGTTGGTACAGTAACTAACCTACAGA 600
AAAAAATCATAACTTATGACCTGATTAATATCATGTGGA 640
GAAGATGAACCTGTCTCGTATGAAAATGGATATTGGCTC 680
AGAGTTCCCAAAGGTGAAGTTGGACTTCTGGTTTGGAAAA 720
TCACACAACCTTACACATTTAATGGCTATGCTGGACCAA 760
GGCTCAGACAGACAAACAAAACCTGACAGATGCTTTTAAG 800

Figure 14A

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AAAGGACACCTCTATTTCAACAGTGGACATCTCTTAATGG 840
 TTGACCATGAAAATTTTCATCTATTTCCACACAGAGTTGG 880
 ACATACATTCOOGGTGGAAAGGGCAAAATGIGGGCAOCCACT 920
 CAAGTTCCTCTATTAAGTTCAGTGGTTCATTTTTTTTCCAA 960
 GGAAGTAAAATGTTTATGGCAGTGCATGGGCCAAGTATAT 1000
 GCAAGTTCCGAATTCGATGGCAATTCGAAATTTTTCAGAAC 1040
 GAAAACCATGCAATTTTCATGCAAGCAATTTTTCAGAAC 1080
 ATTGCTGATAAACCACCTACCTATGCAAGGCOOOGGTTTT 1120
 NTAACAANACAGGACACCATTCAGATCACTGCAATTTTTTA 1160
 AACACOGCAAAATGCAOCTTTGGTGGCAAGGGCTTTTACC 1200
 CNGCTGTCATCAAAAGATGCTTGTATTTTCTTGGCTGACA 1240
 CAGCAAAAATGCTATGCTGCTATGCACTGAGGACATNATATA 1280
 TGCCATTAAGTGTATAAAAACCTGCAATTTTGTATATTTTCC 1320
 GCAAGTAAATTCACATTTTCCACAAACAACTCAATGGAC 1360
 AGCCACTTGTATATAATCCAACTTTTAAATTTCTTTGACATT 1400
 GTGAGCAAAATTTTCTAGCAAAATTTGCATACCCGTAAAGGG 1440
 ACACTTTTTTTAAATTAACAGTTGAGTCTTTTGCAGTAAAAA 1480
 CATTTAGACATTATTTATTTTTCAGTGTGCACTACTGTTT 1520
 GTATTTTGCAAACTGAGCTTGTGTCAGGCAAGGCATTATTT 1560
 TTTAAAAATACTTACTTAAATTAACACACCAACATCTGCA 1600
 AAAAAAAAAAAAAAAAAAAAAA 1622

Figure 14B

hsFATP2 protein sequence

YIYTSGITGLPKAAMITHQRIWYGLTFVSGLKADVIY 40
 ITLFFYHSAALLIGIHGCIIVACATLALRIKFSASQFWDCC 80
 RKYNVIVIQYIGELLRYLONSPQKPNDRDHKVRALGNEL 120
 REDVWRQFVKRFEDICTYEFYAATEGNICFMNYARKVGAV 160
 GRVNYLQKKLTITDILKYDVEKDEPVRDENGVCVRVPKGE 200
 VELVCKKITQLTFNGYACAKAQTEKKKLKRVFKKEDLYF 240
 NSCDLLMVDHENFTYFHDRVGEJFRWKGENVATTEVADIV 280
 GLVDEF 286

Figure 15

hsFATP3 DNA sequence

CAATTGGGGACCCCCAGGGGCACCTGATGGCCACATCTCC 40
 AGGTGAGCCAGGGCAAGTTGCTAAAGCATGCTTTCGGCC 80
 TGGGCATGTTTTCCTTCAACACTGGGGCACTGCTGGCTCGC 120
 GATGACCAAGGTTTTCCTCGCTTCATGATGCTACTGCAC 160

Figure 16A

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ACACCTTCAGGTGCAAGGGGCAATGTGGGCACAACCGA 200
 GGIGGCACAGGTCCTTCAGGCGCTAGATTTTCTTCAGGAG 240
 GTGAACGTCATGCACTCAGTGTGCCAGGGCATGAAGGCA 280
 GGGCTGGCAATGGCAGCGCTAGTTCTGGGTCCCCCCCCACGC 320
 TTTGCACTTATGCACTCTACACCCAGGTGTCTGAGAAC 360
 TTGCCACCTTATGCGCGGGCGCGATTCCTCAGGCTCCAGG 400
 AGTCCTTTGGCCACCAACAGCACTTCAAAACAGCAGAAAGT 440
 TOGGATGGCAAAATGAGGGCTTCGACCCAGCAACCTGTCT 480
 GACCCACTGTACGTTCTGCAACAGGCTGTAGGTGCCCTACC 520
 TGCCCCTCACAACCTGCGCGGTACAGCGCGCTCCTGGCAGG 560
 AAAOCTTCGAATCTGAGCACTTCCACACCTGAGGCAOCTG 600
 AGACAGCAACTCTGTGCGGTGGGGCGGTGGCAGGTGTAC 640
 TGGGCTGTACAGGATCTTTTCTATACAGCACTGGGGTCA 680
 CTATTTTGTAAATAAATGTGGCTGGAGCTGATCCAGCTGTC 720
 TCTGACCTACAAAAA 753

Figure 16B

hsFATP3 protein sequence

QFGTFRGIVWPHLQVSQKLLKDVFRPGDVFFNIGDLLVC 40
 DDQGFILRFHDFRUGDIFRWKGENVATTEVAEVFEALDFLQE 80
 VNVYGVIVPGHEERAGMAALVLRPPHALDLMQLYTHVSEN 120
 LPPYARPRFLRLQESLATTEITFKQKVRMANEGFDPSTLS 160
 DPLVVIDQAVGAYLPLITIRYSALLAGNLR 191

Figure 17

hsFATP4 DNA sequence

TCAAGTACAACCTGCAACGATTGTATATNCATTGGTGAACCTG 40
 TCGCGNIACCTCCTGAAACAGCCACCGCGGGAGGCACAAA 80
 AACAGCACCAGGTTGGCATGGCACTAGGCAATGGCGCTCCG 120
 GCAGTCCATCTGGAACCAACTTTTCCAGCGCTTCCACATA 160
 CCCCAGGIGGCTGAGTTTATAGGGGGCCACAGAGTGCAACT 200
 GTAGCCTGGGCAACTTGGACAGCCAGGTGGGGGCGCTGTGG 240
 TTTCAATAGCGCGATCCTGTCTCTTGTGTACCCCATCCGG 280
 TTGGTAAGGTGTCAACGAGCAACCATGCAAGCTGATCCGGG 320
 GCGCGCAAGCGGTCTGCAATTCCTGCGCAGCTAGGTGAGCC 360
 GGGCCAGCTGGTGGGCGCATCATCCAGAAAGACCCCTG 400
 CGCGGCTTGGATGGCTACCTCAACAGGGGCGCAACAACA 440
 AGAAGATTGCCAAGCATGTCTTCAAGAGGGGGACCAAGGC 480
 CTACCTTACTGGTCAATGTGCTGGTCAATGCAAGCTGGGC 520
 ...

Figure 18A

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TACCTGTACTTCCGACACCGCACTGGGCAACGTTCCGCT 560
 GGAAGGTGACAAAGTGTCCACCAACGAGGTGCAAGGCAC 600
 ACTCAGCCGCTGCTGCAATGGCTCAAGTGGCCGTGTAT 640
 GGTGTCCAGGTGCCAGCAACCAAGGCGGGCCCGCAATGG 680
 CTGCTGTGGCCAGCCCCACTGGCACTGTCACTTGGCAAC 720
 GCTTTGCTCAGGTC 734

Figure 18B

hsFATP4 protein sequence

IGELCRVLLNQPPREAEHQVRMALGNELRQSIWINFSS 40
 RFHIPQVAFFYCAETECNCSLGNFDSQVCAQENSRILSFV 80
 YPIRLVRVNEIDIMELIRCPDGVCIPOQPGEPGQIVGRITQ 120
 KDPLRRFDGYLNQCANNKIAKLVFKKEDQAYLTGVLMVM 160
 DELGYLYFRDRICDIFRWKCEENVSTTEVEGILSRLLDMAD 200
 VAVYGVVEVPGTEG 213

Figure 19

hsFATP5 DNA sequence

CNIGCCTUUTGTACCAAGTCATGGCACTTTGTCTGTGGCA 40
 TCCTCGGCTGCTTACATCTCGGAGCCACCTGTGTCTGGC 80
 CCCCAGTTCTCTACTTCCCTGCTTCTGGCACTGCTGTGG 120
 CAGCATGGCGTCACAGTCATCTGTATGTGGGCGAGCTCC 160
 TGCCTACTTGTGTACATTCCTCCAGCAACCAAGCAACG 200
 CACACATACAGTCCGCTGGCAATGGGCAATGCACTACGG 240
 GCTCATGTGTGGGAGAACCTTCCAGCAGCGTTTGGTCTCT 280
 ATTTCCGATCINGGCAAGTCTTAAGGGCTTCCACAGAGG 320
 GCAACATGGGGCTTTAGTTCACCTATTGTGGGGCGGCTG 360
 CGGGGSCCTGCRGGCAAGATGGAGCTTGGCTCTCTCCGA 400
 TGCCTGTCCCTTTTGAAGCTGGTGCAGTTCACATGCAAGC 440
 GCGGAGGCTGTGAGGCAATCAGGGCTTCTGCATCCCT 480
 GTAGGGCTAGGGGAGCGGGGCTGCTGTGTACCAAGGTGG 520
 TAAGCCAGCAACCTTCTGTGGGCTAACGGGGGCGCGAGA 560
 GCTGTCCGAACGCAAGCTGGTGGCAACGTGGGGCAATCG 600
 GCGCAAGTTTACTACAAACCGGGGAGGTAAGTGGCATGG 640
 ACGGCAAGGCTTCTCTACTTCCGCGACCGACTCGGGGA 680
 CACTTCCGATGCAAGGGCGAGAACGTGTCCACGCAAGAG 720
 GTCAGGGGCGTGTGTGGCAGGTGGACTTCTTGCACAGG 760
 TTAAGTGTATGGCGGTGTGGTGGCAGGTTGTGAGGGTAA 800
 GGTTGGCATGGCTGCTGTGGCATTAGCCCCGGGCACT 840

Figure 20A

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TTGGACGGGGGAGCAAGTTGTACCAGCAAGTTGGGGCTTGGC 880
TCCCTGGCTACGCTACGCCCCATTTTCATCGCATCCAGCA 920
CGCCATGGCAGGTACACAGCAAGTTCAAACTGATCAACACC 960
CGGTTGGTGGCTCAGGGCTTCAATGTGGGGATGGTGGTTG 1000
ACCCCTCTGTTTGTACTGGACAACCGGGGCCAGTCTTCCG 1040
GCCCCCTGACGGGAGCAATGTACCAGGCTGTGTGTGAGGCA 1080
ACCTGGAGGCTCTCATCACTGGCCAACCCACTGGGGTAG 1120
GGATCAAAAGCCAGCCACCCCAACCCCAACACACTGGGTGT 1160
CCCTTTTCATCTGGGCTGTGTGAATCCAGGCTGGCCAT 1200
ACCCCTCAACCTCAGTGGGCTGTGAATCAGTGGGCTGT 1240
TAGCAGTGGCAGATAAACTCAGTGTGTTCACACAAA 1278

hsFATP5 protein sequence

Figure 20B

EGQHGAIVQLLLCALRGPGKDGACILRLSPFELVQFDM 40
EAAEPVRDINQGFCLPGLGEPGLLLTKVVSQQPFVGYREP 80
RELSEKLVNRVROSEVYNTGDLAMDREGLYFRDRL 120
GDTFFAKGENVSTHEVEGVLSDVFLQQVNVYGVCPGCE 160
GKVGMAAVAIAPGQTFDGEKLYQHVRWLPAAYATPHFIR 199

hsFATP6 DNA sequence

Figure 21

CGCTTGTGTGTTAAACAAGAAATTTTCAGCAAGCCAGTTT 40
TGCAGTGACTGCAACAAGTATGATGTGACTGTGTGTTTCA 80
ATATTGGGAGAACITTTGTGGCTACCTTTGCAACAATCTAA 120
GAGACAAGGAGAAAAGCATCATAAGGIGCGTTTGGCAATT 160
GGAAATGGCATACGGAGTCTATGATGCAAGCAATTTTTAG 200
ACAGATTTTGGCAATATAAAGGTGTGTGCAACTTTATGCAGC 240
TACCGAATCAAGCATATCTTTTCATCAACTACACTGGGAGA 280
ATTGGAGCAATTGGGAGACAAATTTGTTTTACAAACTTC 320
TTTCCACTTTTGACTTAATAAAGTATCACTTTACAAAGA 360
TGAACCCATGCAAAATCAGCAGGGTTGGGTATTCATGACA 400
AAAAGGAGACCTGGACTTCTCATTTCTCGAGTCAATGCAA 440
AAAATCCCTTCTTTGGCTATGCTGGGCTTATAAGCACAC 480
AAAAGCACAATTTGCTTTGTGATGTTTTAAGAAGGCAGAT 520
GTTTACCTTAATACTGGAGACTTAATAGTCCAGGATCAGG 560
ACAATTTCCCTTTATTTTTTGGGACGTACTGGAGACATTT 600
CAGATGCAAGGAGCAAAATGTGGCAACCACTGAGGTTGCT 640
GATGTTATTGCAATGTGTGATTTTCATACAGCAAGCAACG 680
TCTATGGGTGTGGCTATATCAGGTTATCAAGCAAGCAGG 720

Figure 22A

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AATGGCTTCTATTATTTTAAAACCAATACATCTTTAGAT 760
 TTGGAAAAAGTTTATCACTAGTTGTACATTTCTAOCAG 800
 CTTATGCTTGTCCACCTTTTTTAAAGATTTCAGCAAAAANT 840
 GCAAGCAACAGCAACATTCAAACTATTCAAGCATCAGTTC 880
 GGGCAACATGCAATTTAATOCACCTCAAAATTTCTCAACCAC 920
 TTTACTTTCATGCATAACTTGA AAAAGTCTTATGTTCTACT 960
 CACCAGGCACTTTTATCATCAATAATGTTAGGGCAATA 1000
 AAACTTTAAAGATTTTTTATATCTACAACTTTTCATATGCTTT 1040
 CTTAGCAACAGCTCAAGGGGGTATATGATTCTTTATCA 1080
 ATGGGCAAGGGAGCTAACATTAATTATGCATGTACTATA 1120
 TTTCCTTAATATCAACATAATTTTTTAAATTGCATAACA 1160
 TTTTAAATTTCTTTTAAATTGATATAAACACAGTTGATTATT 1200
 CTTTTTATCTATTTCGCACTTCAGTGCATAACTAAGTATT 1240
 TTCTTAATACTAAAGATTTTAAATAATAAATAGTGGCTA 1280
 GGGTTTGGCAATCACTAAATAATGTAATTTCTAATAAGT 1320
 AAAATTTCTAATTTTCAATAAAAGATTAATTTTACTCA 1360
 A 1361

Figure 22B

hsFATP6 protein sequence

ACVLKKKFSASQFWSDCCKYDVIVFQYIGELCRYLCKQSKRECEKDKHVR 50
 LAIGNGIRSDWREFLLDRFGNIKVCELYAATESLSFMNYTGRIGATGR 100
 NLFYKLLSIFDLIKYDFQKDERMRNEQGWFMKRRRPELLSRVNAKNPF 150
 FGYAGPYKHKLKLLCNVFKKEDVYLNIGDLIVQDQINFLYFWDRTGDTF 200
 RWKGENVATTEVADVIGMLDFTQFANVYGVAISGYEGRAGVASTILKENT 250
 SLGLEKVYEQVVFILPAYACPRFLRIQEKMEATGTFKLLKHQLVEDGFNP 300
 LKILSEPLYFMDNLKKSIVLLIRELYDQIMLGEIKL 335

Figure 23

mtFATP DNA sequence

TAGTCCATAACGTCAAGCAAGCTCTGCGGGCCTGGCCACC 40
 TTCTGAGGTTGGTCCACCAAGCAATTCCACATTTCCGCAA 80
 CGAATCGAGGGCTTACGTTGTCGATTACTACGGGGGGGCA 120
 CACACAAGGTCAGGCTGATCGAATCGGCAACTCGGATGC 160
 CGCAGTGTGTGGGCAACGCGGGTCAATTGTGGTGGGGCC 200
 AATCAAGGGCTGCTGGCGGGCGGCAATTCAGGGGTG 240
 ATGGCAAGGTTGTCCAGCAAGGGCGGGCTGGCTACGGTG 280
 ACGCAGTCTTCTCAATTCGGGATCAGCAGCTGACCTA 320
 CCGGCAAGCTAACGGCAAGGGCAAGGGTACGGGGGGTG 360

Figure 24A

— *Continued*

Figure 24B

mtFATP protein sequence

msdyvgahttvrlidlatmrvladtpvivrgamtgll 40
arprskasigtvfquraarygdrvflkfgoqgltyrdana 80
tanryaavlaargvggduvgimlmspstvlamlatvkc 120
gaiagmlnyingrgevlahslgllcakvliasesdlvsavae 160
ogasrgrvagduvltvediverfattapatmpasasavgakd 200
tafyiftsgttgfpkasvmtthhrwlralavfgmgllrlkg 240
sdtiysclplyinnaltvavssvinsgatllalgksfsasr 280
fwcavianratafvyigeicryllnqakptdrahgvrvi 320
cngnlrpeiwdetttrfgvarvcefyaaasegnsafinifn 360
vprtagvsnplafvayildtgdlrdsgrvrrvpogeo 400
glllsrvnrlopfogytdqvasekklvinafrqdcwint 440
gumspoomgnaafvdrldgtfrwkgenvattqvaaalas 480
dgtveectvvgvqiprtogragmaaitlragaeofggala 520
rtvyghlpgyalplfvrwvgsлахtttfsrkvalmgay 560
gadiednplyvlagpdegyvpyyaesypeevslgmpog 597

Figure 25

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hsFATP1

1 tcy acc cac ggc gtc cgg gac ccc aaa gca gaa gcc cgc aca gta ggc aca gcy cac cca
61 aga agy gtc caa gaa tct gca gaa aca gaa agy gtc cgc tca ggc tcc tag tcc ctc
121 cct ggc tcc tgc ctc agc ttc tgg gaa act gaa ggc acg gct tgc agc ttc agy atg cgg
M R

181 gct ccy ggt ccy ggc ggc tcc tgg gtc tcy ctc ggc tcy tgg tgg ctc ctc ggc ctc
A P O A G A A S V V S L A L L M L L O L
241 ccy tgg acc tgg agc ccy gca ccy ccy ctc ggc tcy tac tcy ggc agc ggc ggc tgg cgc
P W T W S A A A A L G V Y V G S G O W R

301 ttc ctc ggc atc gtc tgc agc acc ccy agy cga gac ctc ttc ggc ctc tct gtc ctc atc
P L R I V C K T A A R D L F G L S V L I
361 cgc gtc cgc ccy gaa ctc ccy ccy cac caa ggc ggc ctc ggc ctc ggc acc ctc ccy cgc atc ttc
R V R L E L R R H O R A G H T I P R I F
421 caa ggc gta gtc caa gaa caa ccc gaa ggc ctc ggc ctc gtc ggc ggc acc ggc acc ggc ggc
O A V V O R O P E R L A L V D A O T G E
481 tgc tcy acc ttc ccy caa ctc gac ggc tac tcc aat ggc gta ggc aac ctc ttc cgc ctc
C W T F A O L D A Y S N A V A N L F R O
541 ctc ggc ttc ggc ccy ggc gac gtc gtc ggc atc ttc ctc gaa ggc ccy ccy gaa ttc gtc
L G F A P F G D V V A I F L E G R P E F V
601 ggc ctc tgc ctc ggc ctc ggc acc ggc ggc atg gaa ggc ggc ctc ctc aac gtc aac ctc
G L N L G L A K A G H E A A L L M V M L
661 ccy ccy gaa ccc ctc ggc ttc tgc ctc ggc acc tcy ggc ggc aag ggc ctc atc ttc ggc
R R E P L A F C L G T S G A K A L I F G
721 gaa gaa atg gtc ggc ggc gtc ggc gaa gtc agc ggc cat ctc ggc aaa agt ttc atc aag
G E M V A A V A E V S G H L G K S L I K
781 ttc tgc tct gaa gac ttc ggc ccc gaa ggc atc ttc ccy gac acc ctc ctc ctc gac ccy
F C S G D L G F E G I L P D T H L L D P
841 ctc ctc aag gaa ggc tct act ggc ccc ttc gca caa atc ccc agc aag ggc atg gac gac
L L R E A S T A P L A O I P S K G M D D
901 ggc ttc ttc tac atc tac agc tcy ggc acc acc ggc ctc ccc aag ggc ggc atc ggc gtc
R L F Y I Y T S G T T G L P K A A I V V
961 cgc agc agy tac tac ggc atg gca ggc ttc ggc ctc ctc tac cgc atg cgc ggc ggc
H S R Y Y R M A A F G H H A Y R M O A A
1021 gac gtc ctc tac gac tgc ctc ctc ctc tac ctc ctc gca gaa aac atc atc ggc gtc ggc
D V L Y D C L F L Y H S A G N I I G V G
1081 caa gtc ctc atc tac ggc ctc gca gtc gtc ctc ctc agc aaa ttc tcy ggc agc ggc ttc
O C L I Y G L T V V L R R K F S A S R F
1141 tgg gac gac ggc atc aag tac aac tgc agc gtc gtc caa gac atc ggc gaa atc tgc cgc
W D D C I K Y N C T V V O Y I G E I C R
1201 tac ctc ctc aag caa ccy gtc cgc gaa ggc gaa agy cga cgc gtc cgc ctc ggc gtc
Y L L K O P V R E A E R R H R V R L A V
1261 ggc aac ggc ctc ggc ctc ggc atc tgc gaa gaa ttc agc gaa ggc ttc ggc gta ggc caa
G N G L R P A I W E E F T E R F G V R O
1321 atc ggc gaa ttc tac ggc ggc acc gaa tgc aac tgc agc atc ggc aac atg gac ggc aag
I G E F Y G A T E C N C S I A N H D G K
1381 gtc ggc ttc tgc ggc ttc aac agc ggc atc ctc ccc ctc tac ccc atc ccy ctc gtc
V G S C G F N S R I L P H V Y P I R L V
1441 aag gtc aat gaa gac aca atg gaa ctc ctc ccy gac ggc cgc gaa ggc ctc tac atc ttc tgc
K V H E D T H E L L R D A O G L C I P C
1501 caa ggc ggc ggc ctc ggc ctc ctc gtc ggc caa atc aac caa caa ggc ccy ctc ggc cgc
O A G E P G L L V G O I N O O D P L R R
1561 ttc ggc ggc tac gtc agc gaa agc ggc acc agc aag aag atc ggc tac agc gtc ttc agc
F D G Y V S E S A T S K K I A H S V F S
1621 aag ggc gac agc ggc tac ctc tca ggc gac gtc cta gtc atg gac gaa ctc ggc tac atg
X G D S A Y L S G D V L V M D E L G Y M
1681 tac ttc ccy gac ggc agc ggc gac acc ttc cgc tgg cga ggc gaa aac gtc tcc acc acc
Y F R D R S G D T F R W R G E N V S T T
1741 gaa gtc ggc gtc ctc agc cgc ctc ctc ggc caa aca gac gtc ggc gtc tat ggc gtc
E V E G V L S R L L G O T D V A V Y G V
1801 ggc gtc cca gaa gtc gaa ggc aag gca ggc atg ggc ggc gtc gca gac ccc ctc agc ctc
A V P G V E G K A G H A A V A D P H S L
1861 ctc ggc ccc aac ggc aca tac caa ggc ctc caa aag gtc ctc gca ccc tat ggc ccy ccc
L D P N A I Y O E L O K V L A P Y A R P
1921 atc ttc ctc ggc ctc ctc ccc caa gtc gac acc aca ggc acc ttc aag atc caa aag agc
I F L R L L P O V D T T G T F K I O K T
1981 agy ctc caa gaa ggc ggc ttc gac cca cgc caa acc tca gac ccy ctc ttc ttc ctc gac
R L O R E G F D P R O T S D R L F F L D
2041 ctc aag caa ggc ctc tac ctc ccc tca aat gaa gca gtc tac act cgc atc tgc tcy ggc
L K O G H Y L P L N E A V Y T R I C S G
2101 ggc ttc ggc ttc tga agc tgc ttc tct act ggc cca aaa ctc tgg ggc tgg tgg gaa agy
A F A L

2161 cca ggc tga ggc aca caa ggc tgc cca ggc gtc ggc tac tac aca ccc acc tgg ccy
2221 agc tgc acc tgg cgc gca tcc tgg act gaa aac ctc gaa ctc caa agy aac ccy tgc
2281 ctc tct ggc ggc tgc gtc ctc tgc tgc ctc ctc ctc ctc ttc caa ctc ctc ttc
2341 ctc ttc atc ctc gtc ctc gtc tgc tgc tgc tgc tgc ttc ttc ttc ttc ttc
2401 ttc ttc ttc ttc aag atc gaa tct cac tct gtc ggc ccy ggc aag gtc tgg tgg ggc
2461 ctc ggc tca ctc caa ctc ctc ctc ggc gtc caa gtc atc ctc ctc caa ctc ctc
2521 gaa tag ctc gaa tca caa gca ccc ggc acc agc tcc agc taa ttc tta tat ttc tag tag
2581 aca ggc ggc ttc acc atg tgc agy ctc gtc ttc aac tcc tga ctc ctc agc ctc
2641 tgg ctc ccy ctc ctc aca gtc ctc ggc tta tag ggc tga ggc tct ggc ccy ggc ttc ctc
2701 ttc ttc ttc ctc ctc ctc ccy agy gtc gaa cac agc tgc ctc ggc agc tgc atc ttc tgc
2761 agy gtc caa ctc ttc ttc ggc acc gca gaa atc atc ttc ctc ggc ctc tgg acc ccy acc
2821 ggc ggc tcc cca ctc ctc ctc ccy ctc tgc ttc agy ggc ccc caa tcc agy ctc ctc
2881 ggc gtc ggc ttc caa atg ctc caa gtc ctc cat gtc act tcc aag caa ggc ctc ctc ctc
2941 tgc tga atg gaa ggc ccy ggc gtc ccc cgc ggc aac tgg aaa atc tcc caa ggc agy cca
3001 atc ggc ttc tgc acc tcc ccy ttc ctc tca cat ttc ctc agc ccc acc ttc ccc tcc tga
3061 ggc ggc gaa agc ttc ccy aat tga ctc tga cca ctc gaa tgc cac ctc tgc caa ctc
3121 ctc tga tgc ctc cat tta ggc atc tcc atg gaa ctc ctc ctc gaa ggc ctc gaa ccc tgc
3181 acc ccy tgg ctc ctc agc caa ctc ctc gtc ctc ggc ggc ggc ttc ctc ggc gtc ttc
3241 atc tgg tgc gtc tac tgg agy gtc cca caa gaa agy caa gaa agy ggc caa ggc agy ttc
3301 ctc ggc ggc ttc tgc ctc aag ctc caa ggc ttc tag ctc gtc gaa tat acc cca ctc
3361 ggc ggc tgg ctc ctc tga tgc ccc cat tga tgg ctc tga cac gtc gtc ggc ggc gac gtc
3421 cca gac aac ccc acc agy agy ggc caa tcc cta ctc gtc tcy ctc gtc gtc cat ctc
3481 gaa cat cca cgc caa ctc ttc tgg ggc ccy cca ccc agy ccy cca ggc cgc ctc tcc tcc
3541 ctc caa caa ccc ctc tgg ggc ctc ggc ggc ggc ggc cca tgg gaa gaa cca ccy tgg ctc
3601 ctc atg tga act ttc ctc ggc act gtc gtc tta ttc ctc aat tga ttc aag aaa taa acc
3661 tga aca ccy ctc ggc gaa aaa aaa aaa aaa agy ccy ggc gtc

Figure 26

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hsFATP4

[illegible]

Figure 27

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Protein sequence 646 a.a. MPAPGAGAAASV ... VYTRICSGAPAL

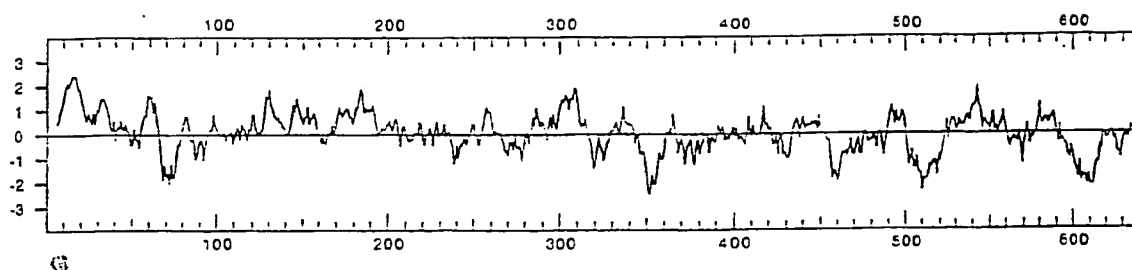


Figure 28A

Protein sequence 646 a.a. MPAPGAGAAASV ... VYTRICSGAPAL

646 Amino Acids MW : 71062 Dalton

		n	n(%)	MW	MW(%)	
A	ala	alanine	64	9.5	4546	6.4
C	cys	cysteine	15	2.3	1545	2.2
D	asp	aspartic acid	30	4.6	3450	4.9
E	glu	glutamic acid	31	4.8	4000	5.6
F	phe	phenylalanine	29	4.5	4264	6.0
G	gly	glycine	63	9.8	3592	5.1
H	his	histidine	13	2.0	1781	2.5
I	ile	isoleucine	29	4.5	3279	4.6
K	lys	lysine	22	3.4	2818	4.0
L	leu	leucine	77	11.9	8707	12.3
M	met	methionine	11	1.7	1441	2.0
N	asn	asparagine	15	2.3	1710	2.4
P	pro	proline	29	4.5	2814	4.0
Q	gln	glutamine	35	5.5	3201	4.5
R	arg	arginine	49	7.6	7648	10.8
S	ser	serine	33	5.1	2872	4.0
T	thr	threonine	27	4.2	2728	3.8
V	val	valine	51	7.9	5055	7.1
W	trp	tryptophan	9	1.4	1674	2.4
X	unk	unknown	-	-	-	-
Y	tyr	tyrosine	24	3.7	3913	5.5
Z	---	STOP	-	-	-	-

Figure 28B

23/117

11

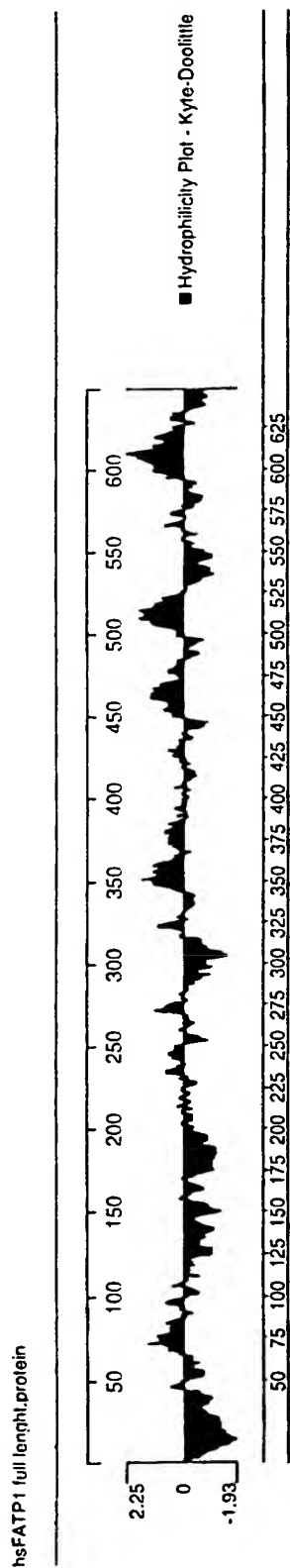


Figure 28C

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hsFATP4.pep -> KD Hydrophobicity <11/1>

Protein sequence 643 a.a. MLIGASLVGVLL ... AYSRIQAGEEKL

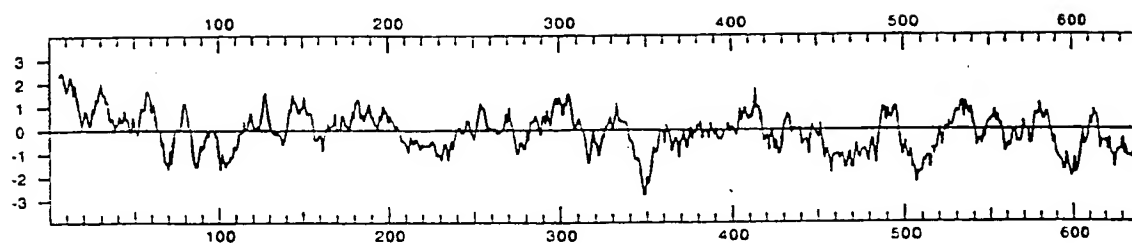


Figure 29A

hsFATP4.pep -> A. A. Usage

Protein sequence 643 a.a. MLIGASLVGVLL ... AYSRIQAGEEKL

643 Amino Acids MW : 72018 Dalton

		n	n(%)	MW	MW(%)
A ala	alanine	46	7.2	3267	4.5
C cys	cysteine	16	2.5	1648	2.3
D asp	aspartic acid	33	5.1	3795	5.3
E glu	glutamic acid	33	5.1	4258	5.9
F phe	phenylalanine	34	5.3	5000	6.9
G gly	glycine	54	8.4	3079	4.3
H his	histidine	12	1.9	1644	2.3
I ile	isoleucine	30	4.7	3392	4.7
K lys	lysine	31	4.8	3970	5.5
L leu	leucine	76	11.8	6594	11.9
M met	methionine	12	1.9	1572	2.2
N asn	asparagine	21	3.3	2394	3.3
P pro	proline	31	4.8	3008	4.2
Q gln	glutamine	23	3.6	2945	4.1
R arg	arginine	45	7.0	7024	9.8
S ser	serine	35	5.4	3046	4.2
T thr	threonine	32	5.0	3233	4.5
V val	valine	46	7.2	4557	6.3
W trp	tryptophan	8	1.2	1488	2.1
X unk	unknown	-	-	-	-
Y tyr	tyrosine	25	3.9	4076	5.7
Z ---	STOP	-	-	-	-

Figure 29B

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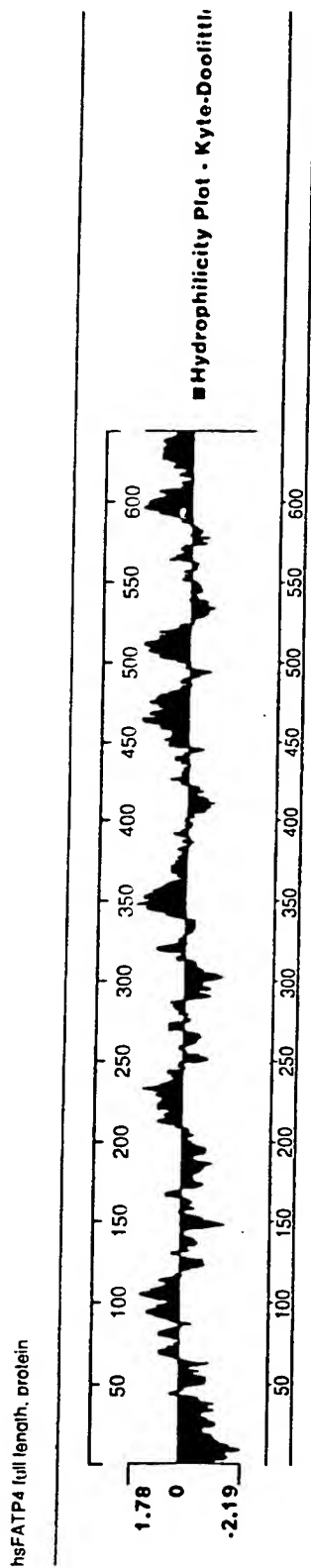


Figure 29C

Page 1

[illegible]

Figure 30A

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Page 2

Decoration 'Decoration #1': Shade (with solid bright yellow) residues that match the consensus named 'Consensus #1' exactly.

Figure 30B

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Alignment Report of Unaligned, using Clustal method with PAM250 residue weight table.

Page 1

1	MDRAAEGAGG AASV VIEDA LMA LINGH LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	hsFAT1pep
1	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	mmFAT1pep
61	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	hsFAT1pep
61	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	mmFAT1pep
121	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	hsFAT1pep
121	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	mmFAT1pep
181	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	hsFAT1pep
181	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	mmFAT1pep
241	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	hsFAT1pep
241	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	mmFAT1pep
301	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	hsFAT1pep
301	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	mmFAT1pep
361	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	hsFAT1pep
361	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	mmFAT1pep
421	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	hsFAT1pep
421	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	mmFAT1pep
481	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	hsFAT1pep
481	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	mmFAT1pep
541	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	hsFAT1pep
541	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	mmFAT1pep
601	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	hsFAT1pep
601	MDRAAEGAGG TAAV AISHA LPHITWESATATAN L GMYAVG SGGHRELEETINCAKTAAPD LDCILSSV	mmFAT1pep

Decoration 'Decoration #2': Shade (with solid bright yellow) residues that match the consensus named 'Consensus #1' exactly.

Figure 32

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hsFATP6

```

1      AAC GGC AAG TAA GTG CAA GTC AAT TAA TGT GAG TAA CTT ACT CAT TAA GCA CTT CAG GCT
61     TTA CAC TTT ATG CTT CCG GTC TGT TAT GTT GTG TGG AAT TGT GAG CCG ATA CCA ATT TCA
121    CAC ACG AAC CAG CTA TGA CAT GAT TAC CAA TTT AAT ACG ACT CAC TAT ACG GAA TTT GGC
181    CCT CCA GGC CAA GAA TTT GTC ACG ACG GGT GTC GAG CTT CCG GGC TTT TGG TGT GTA
241    GAG ACT TTA AAT CAC TGT GTC TCT CAG TCA TCA TCC CAG CTT TTT CCG GTC TGA ATT
301    CAG CTT TCA ACT CAA GTC CAC GGT AAA GAT TAC CAG CAG GGA GAA AAG CTT CAG TTT CAG
361    GAC TTT TTT CAG ACG GTG GAG TCG GAG GTC CTT TGT TTT TCA GTC GTC CAG TGA CTT AAG
421    CTT AAT TTT CAG CAC CAC TTT GGT CCA CTT TTT TGT TGT AAA CTT ACG ATT CAG TTT CTT
481    ACG ATT CTT CTT CAC CTT CTT TGT CTT CCG AAA ACG TGA CAA GAA CTT CAG GTG TAA GTC
541    CCG AAT ATT GAG GAT CTT CCG TCT CCG TGT AAG GTC CTT CTT GGA GAA GAA CCG TGT
601    TGT GGT CAG GGA TCA GAG CTT TCT TCT GTC CCA GTC CTT CTT CTT CTT CTT CTT CTT CTT
      N L L S M L
661    ACA GTT CTA GTT GTC GCA ATC GTC GTC CTT CAC TTT TGT CAG AAA CTT CTT CTT CTT CTT
      T V L G A G M V V L M P L Q X L L F P Y
721    TTT TGT GAT CAC TTT TGT TTT CTT TGT AAG GTG GTG CTT ACT ATA TTT CCG CTT AAG AAG
      F V D D F W F V L E V V L I I I F L R K
781    TAT GAA AAG GGA GTG GAG CTT GTC TGT CTT CTT AAG TTT CTT AAG CTT AAG AAG AAG
      Y R X R G E L V T V L D K F L S H A E F
841    CAA CTT TGT AAG CTT TTT ACT ACT TAT GAG GGA GAT ACT TAT TAT TAT TAT TAT TAT TAT
      Q P R R P P I I Y E G D I Y T Y Q D V D
901    AAA ACG GTC AAT GTC GTC CAC GTC TTT CTT AAG CTT TTT TTT TTT TTT TTT TTT TTT
      R R S S R V A H V P L N H S S L R X G C
961    ACG GTG GTC CTT CTT ACG AAT GAG CCG GAT CTT CTT CAG GTG TGT TTT GTC CTT CTT
      T V A L L M S N E P D F V N V W P G L A
1021   AAG CTT GTC TGT GTC GTC TTT CTT AAT AAT AAT CTT CTT TTT AAT CTT CTT CTT CTT
      K L G C V V A F L N T N I R S N S L L N
1081   TGC AAT CTT CTT TGT GTC GTC GTC CTT CCA GTC CTA GTC GTC GTC GTC GTC GTC GTC
      C I P A C G P R A L V V G A D L L G T V
1141   GAA GAA ATT CTT CCA AAT CTT TCA GAA AAT ATT GTC TGT GTC AAT AAT GAT TTT GTC
      E E I L P S L S E N I S V W G M F D S V
1201   CCA CAA GTT CTA ACT TCA CTT AAA GAA AAA CTT AAT CTT TCA CTT GAT CAG CTT CTT CTT
      P Q G V I S L K E K L S T S P D E P V F
1261   CCG AAT CAC CAT GTC GTC TCA CTT CTT AAT CTT CTT CTT CTT CTT CTT CTT CTT CTT
      R S H N V V S L L N S T C L Y I F T S G
1321   ACA ACA GTC CTA CCA AAA GTC GTC ACT AAT CAG CAG CAG GTC TTA AAG GTC TGT GTC
      T T G L F K A A V I S Q L Q V L R C A
1381   GTC CTT TGT TTT TTT GTC TGT ACT GTC CTT CTT TAT TAT TAT TAT TAT TAT TAT TAT
      V L W A F G C T A H D I V Y I T L P L Y
1441   CAT AAT TCA CCA GTC ACT CTT GGA ATT TTT GGA TGT GTC GAG TGT GTC ACT TGT GTC
      H S S A A I L Q I S G C V E L G A T C V
1501   TCA AAG GAT AAT TTT TCA CCA AAT CAG TTT TGT AAT CAC CTT AAG AAT TAT GAT TGT ACT
      L R K K F S A S Q F W S D C K K Y D V T
1561   CCG TTT CAG TAT ACT GGA GAA CTT TGT CCG TAT CTT TGT AAA CAA TTT AAG GGA GGA GGA
      V F Q Y I G E L C R Y L C K Q S R R E G
1621   GAA AAG GAT CAT AAG GTG CTT TGT GCA ATT GGA AAT GTC AAT CCG AAT GAT TTA TGT AAG
      E R D H K V R L A I G N G I R S D V W A
1681   GAA TTT TTA GAT AAT TTT GGA AAT TTA AAG GTG TGT GAA CTT TAT TCA GTC ACT GAA TCA
      E F L D R P G N I K V C E L Y A A T E S
1741   AAT AAT TTT TTT AAT TAT ACT CCG AAT ATT GGA GCA ATT GGT AAT AAT TTT TTT TTT
      S I S F M N Y T G R I G A I G R T N L F
1801   TAT AAA CTT CTT CTT CTT CTT CTT CTT CTT CTT CTT CTT CTT CTT CTT CTT CTT CTT
      Y R L L S T F D L I K Y D F Q K D E P M
1861   AAT AAT CAG CAG GTC TGT TTT CTT CTT CTT CTT CTT CTT CTT CTT CTT CTT CTT CTT
      R N E Q G W C I H V K R G E P G L L I S
1921   CCA GTG AAT CCA AAT CTT CTT CTT CTT TAT GTC GTC CTT CTT CTT CTT CTT CTT CTT
      R V N A K N P F F C Y A G P Y K H T K D
1981   AAT TGT CTT TGT GAT GTC TTT AAG AAG GGA GAT TAT TAT TAT TAT TAT TAT TAT TAT
      K L L C D V F K K G D V Y L N T G O L I
2041   GTC CAG GAT CAG GAT AAT TTT CTT TAT TTT TGT GAT CTT ACT GGA GAT ACT TTT AAT TGT
      V O D Q D N F L Y F W D R T G D T F R W
2101   AAA GGA GAA AAT GTC GCA ACT ACT GAG GTC GTC GAT ACT GGA AAT TGT GAT TTT AAT
      K G E N V A T T E V A D V I G M L D F I
2161   CAG GAA GCA AAT GTC TAT GTC GTC GTC GTC TAT TAT GAA GGA GGA GCA GGA AAT GTC
      Q E A N V Y G V A I S G Y E G R A G M A
2221   TTT ATT TTT TTT AAA CCA AAT CCA TTT TTA GAT TGT GAA AAA GTC TAT GAA CAA GTC TTA
      S I I L K P N T S L D L E K V Y E Q V V
2281   AAT TTT CTA CCA GTC TAT GTC TGT CCA CCA TTT TTA AAT TAT CAG GAA AAA AAT GGA GCA
      T F L P A Y A C P R F L R I Q E R H E A
2341   AAT GGA AAT TTT AAA CTA TGT AAT CAT CAG TGT GTC GAT GAT GAT TTT AAT CCA CTT AAT
      T G T F K L L K H O L V E D G F N P L K
2401   ATT TTT GAA CCA CTT TAT TAT AAT TTT AAT TTT AAT TTT AAT TTT AAT TTT AAT TTT
      I S E P L Y F M D N L K K S Y V L L T R
2461   GAA CTT TAT GAT CAA ATA AAT TTA GGT GAA AAT CTT TAT GAT TTT TAT TAT TAT TAT
      E I Y D Q I M L G E I K L
2521   TTT CTT TTT TTT TTT TAT GAA GAA TGA GGT GGT GGT GGT TAT TAT TAT TAT TAT TAT
2581   AAG GGA GTC AAT ATT AAT TAT CCA TAT ACT ATA TTT CTT TAT TAT TAT TAT TAT TAT
2641   AAT TGT TTA AAT TTT TAT TTT TTT TTT TTT TTT TTT TTT TTT TTT TTT TTT TTT
2701   ACT TAT TGT GAT ATT CAG TGT TAT ACT AAT TAT TAT TAT TAT TAT TAT TAT TAT TAT
2761   AAT AAT GTC TGT TGT TGT TGT TGT TGT TGT TGT TGT TGT TGT TGT TGT TGT TGT
2821   TAT AAT TTT GAA TAA AAT ATT AAA TTT TAT TAT TAT TAT TAT TAT TAT TAT TAT TAT
2881   GTC GT

```

Figure 34

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Protein sequence 619 a.a. MLISWLTVLGAG ... LYDDMLGEEKL

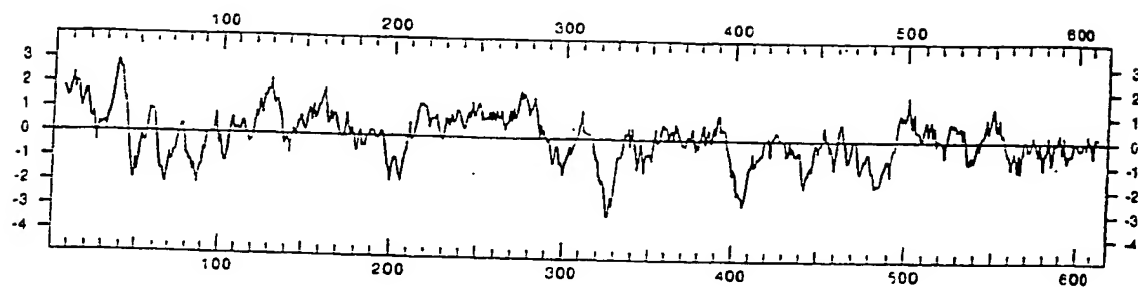


Figure 35A

Protein sequence 619 a.a. MLISWLTVLGAG ... LYDDMLGEEKL

619 Amino Acids MW : 70066 Dalton

		n	n (%)	MW	MW (%)
A	ala	33	5.3	2344	3.3
C	cys	14	2.3	1442	2.1
D	asp	34	5.5	3910	5.6
E	glu	31	5.0	4000	5.7
F	phe	34	5.5	5000	7.1
G	gly	44	7.1	2508	3.6
H	his	13	2.1	1781	2.5
I	ile	37	6.0	4184	6.0
K	lys	48	7.8	6148	8.8
L	leu	75	12.1	6481	9.3
M	met	11	1.8	1441	2.1
N	asn	21	3.4	2394	3.4
P	pro	21	3.4	2038	2.9
Q	gln	16	2.6	2305	3.3
R	arg	27	4.4	4214	6.0
S	ser	40	6.5	3481	5.0
T	thr	30	4.8	3031	4.3
V	val	51	8.2	5052	7.2
W	trp	11	1.8	2046	2.9
X	unk	-	-	-	-
Y	tyr	26	4.2	4239	6.1
Z	---	-	-	-	-

Figure 35B

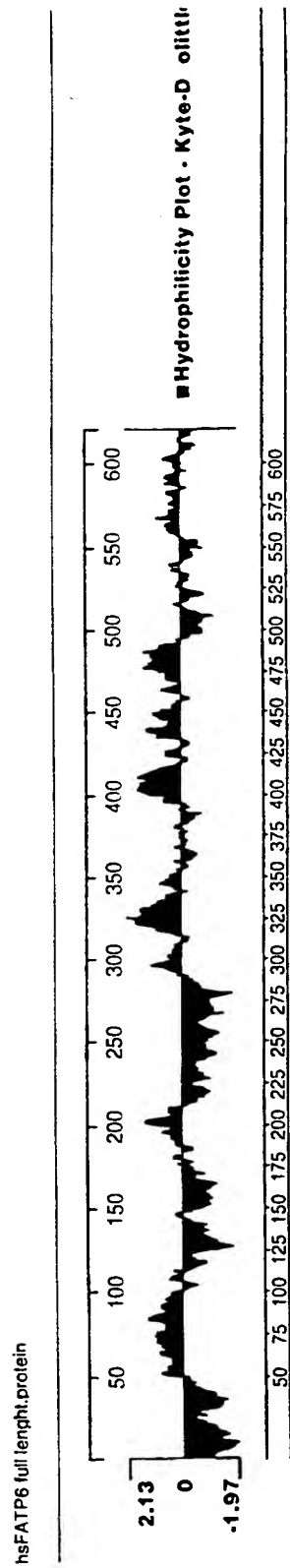


Figure 35C

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Alignment Report of hFATP1,4,6 Alignment, using Clustal method with PAM250 residue weight table.

Page

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1  LHRAF--GACAAISVSSLAALLWLHGGPQWTSASAAAGGVVIGSGGCGWREPRIVCQNEAHPHRLHNSL  hsFATP1pep
1  L-----FSGKQ-VQKSLWTEOVGHSLSLFLXLGSGCGWREPRIVCQNEAHPHRLHNSL  hsFATP4pep
1  HLLSWLTVLGGGCHVHHLQKLFIEYFDDH-----LWVVKM-----  hsFATP6pep

59  SVAIRERRELELRHORAGHELIRIRIOAVOQICPELDAIVDAIGECNTEAQLNDARSHNAFSS  hsFATP1pep
46  LVLKKAQKAVROCLORRATVIRI LSAATSRIRHEDDTATATFIEGTDTHHNSEREDTAEVSS  hsFATP4pep
38  -VLLIIISLKKYKRGIELVQWLDKELSHAKRGQEPFPIIDYIEG--DIYATYODVIDKRISLR  hsFATP6pep

119 -LFRQLGFPAPGQWVATIRLIEGDEETATVGLNLCQDNRHAKMPEATIRGVNTEARPEPIA  hsFATP1pep
106 -LQOARKQENSGIDVAATIRNTERNNAESVGLNLEGMARKTGVVETATDIPKNDNRDAITLH  hsFATP4pep
95  VGLNHSSEKKKQSTVALLLSNDEEDLVHVFLLASLQGCVAFTENONIRSNSSKNEGIRAC  hsFATP6pep

178  LQVIGCGVVAQVAAEASGNGCKLEIKKQSGDALGHEIILSDHLLHTEFSSQCEASTAFEL  hsFATP1pep
165  LQVIGCGVVAQVAAEASGNGCKLEIKKQSGDALGHEIILSDHLLHTEFSSQCEASTAFEL  hsFATP4pep
155  LQVIGCGVVAQVAAEASGNGCKLEIKKQSGDALGHEIILSDHLLHTEFSSQCEASTAFEL  hsFATP6pep

238  LQVIGCGVVAQVAAEASGNGCKLEIKKQSGDALGHEIILSDHLLHTEFSSQCEASTAFEL  hsFATP1pep
224  LQVIGCGVVAQVAAEASGNGCKLEIKKQSGDALGHEIILSDHLLHTEFSSQCEASTAFEL  hsFATP4pep
211  VVSLKSTCLVAFSSQSTIGLTPACAVISOLOVLGSA-LVWAGGCTAHNDEVLITAFH  hsFATP6pep

296  LQVIGCGVVAQVAAEASGNGCKLEIKKQSGDALGHEIILSDHLLHTEFSSQCEASTAFEL  hsFATP1pep
282  LQVIGCGVVAQVAAEASGNGCKLEIKKQSGDALGHEIILSDHLLHTEFSSQCEASTAFEL  hsFATP4pep
270  AALIGLNSGSCVLELQACVILKQKQSSAISQSLHSLQKQKDVGVVPSYVIGELQCEV  hsFATP6pep

356  LQVIGCGVVAQVAAEASGNGCKLEIKKQSGDALGHEIILSDHLLHTEFSSQCEASTAFEL  hsFATP1pep
342  LQVIGCGVVAQVAAEASGNGCKLEIKKQSGDALGHEIILSDHLLHTEFSSQCEASTAFEL  hsFATP4pep
330  LQVIGCGVVAQVAAEASGNGCKLEIKKQSGDALGHEIILSDHLLHTEFSSQCEASTAFEL  hsFATP6pep

416  LQVIGCGVVAQVAAEASGNGCKLEIKKQSGDALGHEIILSDHLLHTEFSSQCEASTAFEL  hsFATP1pep
402  LQVIGCGVVAQVAAEASGNGCKLEIKKQSGDALGHEIILSDHLLHTEFSSQCEASTAFEL  hsFATP4pep
390  LSTFDLILYDFOKDIEPMHNELOGWASLHVKKQSGDALGHEIILSDHLLHTEFSSQCEASTAFEL  hsFATP6pep

475  LQVIGCGVVAQVAAEASGNGCKLEIKKQSGDALGHEIILSDHLLHTEFSSQCEASTAFEL  hsFATP1pep
461  LQVIGCGVVAQVAAEASGNGCKLEIKKQSGDALGHEIILSDHLLHTEFSSQCEASTAFEL  hsFATP4pep
447  LQVIGCGVVAQVAAEASGNGCKLEIKKQSGDALGHEIILSDHLLHTEFSSQCEASTAFEL  hsFATP6pep

534  OTQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQV  hsFATP1pep
520  HADQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQV  hsFATP4pep
506  IOEAQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQV  hsFATP6pep

593  TIGVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQV  hsFATP1pep
579  KETGCTYKFGKQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQV  hsFATP4pep
566  AIGVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQVQV  hsFATP6pep

```

Decoration 'Decoration #1': Shade (with solid bright yellow) residues that match the Consensus exactly.

Figure 36

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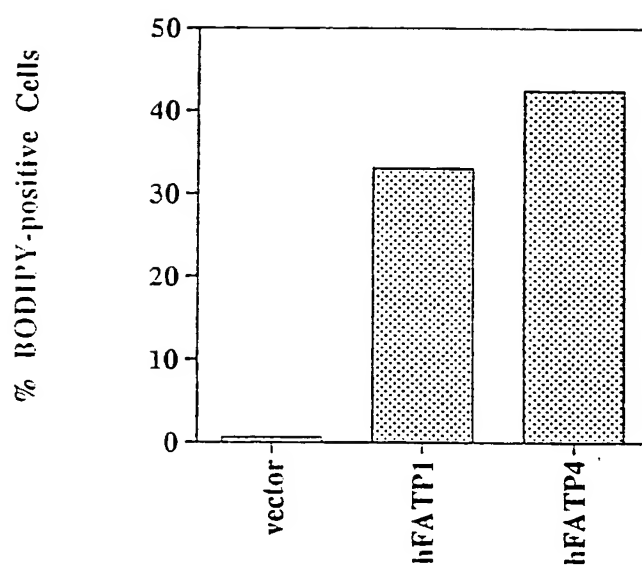
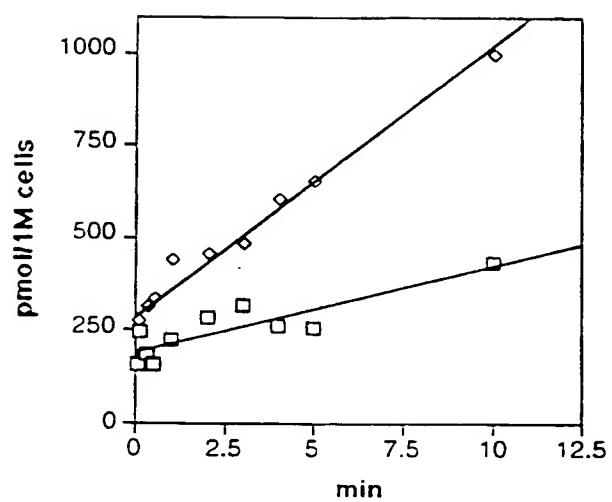


Figure 37

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- 293 vector control: 23 pmol/(min*1*10⁶ cells)
◇ 293 FATP4 clone 7: 73 pmol/(min*1*10⁶ cells)

Fig. 38

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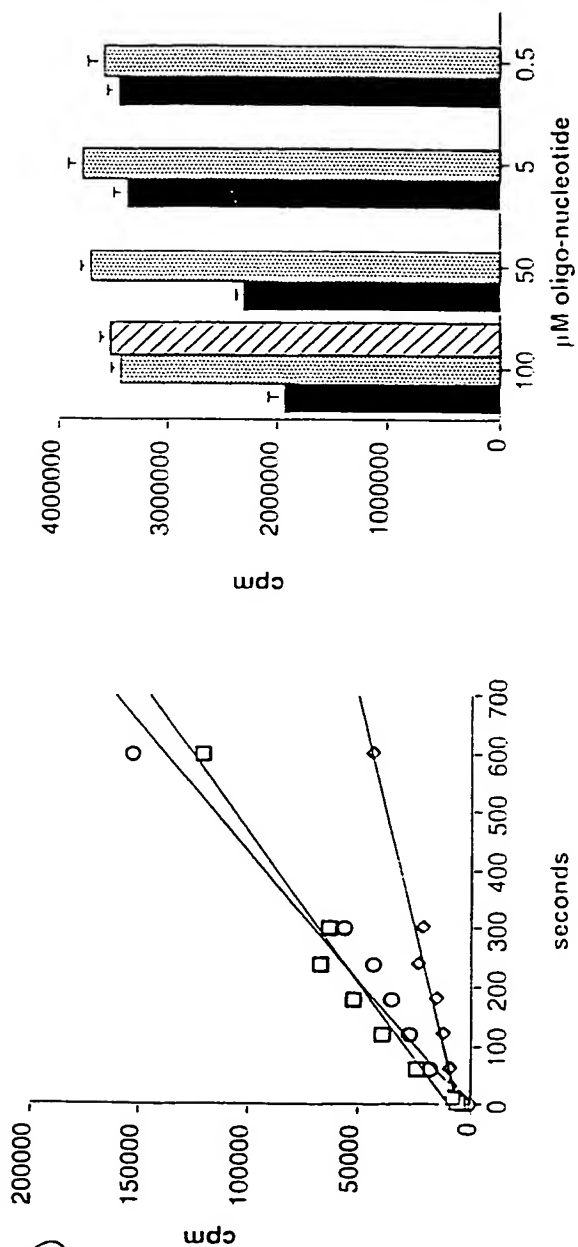


Fig. 40

Fig. 41

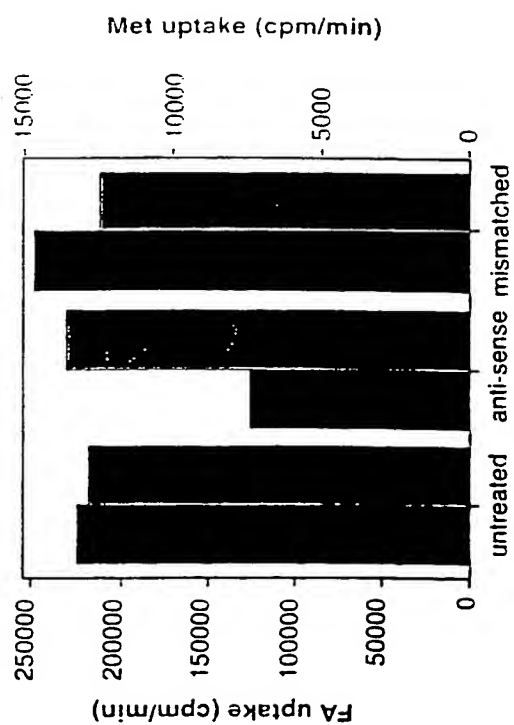
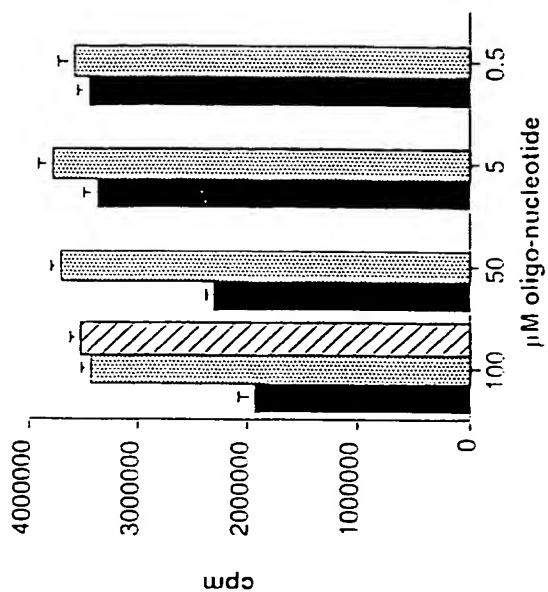


Fig. 42

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mmFATP4 DNA sequence

ATGCTGCTTGGAGCCTCTCTGGTGGGGGCGCTACTGTTCTCCAAGCTAGTGTCTGAAGCTGCCCTGGACCCAGGTGGGATT
 CTCCCTGTTGCTCCTGTACTTGGGGTCTGGTGGCTGGCGTTTCATCCGGGTCTTCATCAAGACGGTCAGGAGAGATATCT
 TTGGTGGCATGGTCTCTCAAGGTGAAGACCAAGGTGCGACGGTACCTTCAGGAGCGGAAGACGGTGCCCTGCTGTTT
 GCTTCAATGGTACAGCGCCACCCGGACAAGACAGCCCTGATTTTCGAGGGCACAGACACTCACTGGACCTTCCGCCAGCT
 GGATGAGTACTCCAGTAGTGTGGCCAACCTTCTGCAGGGCCCGGGGCTGGCTCAGGCAATGTAGTTGCCCTCTTTATGG
 AAAACCCCAATGAGTTTGTGGSTCTGTGGCTAGGCATGGCCAGCTGGGGCGTGGAGGCGGCTCTCATCAACACCAACCTT
 AGGCGGGATGCCCTGCGCCACTGTCTTGACACCTCAAAGGCACAGCTCTCATCTTTGGCAGTGAGATGGCCTCAGCTAT
 CTGTGAGATCCATGCTAGCCTGGAGCCCACTCAGCCTCTTCTGCTCTGGATCCTGGGAGCCCAAGCAGTGCCCTGCA
 GCACAGAGCATCTGGACCTCTTCTGGAAGATGCCCCGAAGCACCTGCCAGTCACCCAGACAGGGSTTTTACAGATAAG
 CTCTTCTACATCTACACATCGGGCACCACGGGGCTACCCAAAGCTGCCATTGTGGTGCACAGCAGGTATTATCGTATGGC
 TCCCTGGTGTACTATGGATTCCGCATGCGGCTGTAGCATTGTCTATGACTGCCCTCCCCCTCTACCACTCAAGCAGGA
 AACATCGTGGGGATTGGCAGTGCTTACTCCACGGCATGACTGTGGTGATCCGGAAGAAGTTCTCAGCCTCCCGGTTCTGG
 GATGATTGTATCAAGTACAAGTGCACAGTGGTACAGTACATTGGCGAGCTCTGCCGCTACCTCCTGAACCAAGCACCCTG
 TGAGGCTGAGTCTCGGCACAAGGTGCCATGGCATGGCACTGGGCAACGGTCTCCGGCAGTCCATCTGGACCGACTTCTCCAGCC
 GTTTCACATCCCCCAGGTGGCTGAGTTCTATGGGGCCACTGAATGCAACTGTAGCTGGGCAACTTTGACAGCCGGGTG
 GGGGCTGTGGCTTCAATAGCCGCATCCTGTCTTTGTGTACCTATCCGTTTGGTACGTGTCAATGAGGATACCATGGGA
 ACTGATCCGGGGACCCGATGGAGTCTGCATTCCCTGTCAACCAAGGTCAAGCAGGCCAGCTGGTGGGTGCGATCATCCAGC
 AGGACCTCTCCGCCGTTTTCGACGGGTACCTCAACCAAGGTGCCAACAAGAAAGATTGCTAATGATGTCTTCAAGAG
 GGGGACCAAGCTACCTCACTGGTGAGCTCCTGGTGTGGATGAGCTGGGTTACCTGTACTTCCGAGATCGCACTGGGGA
 CACGTTCCGCTGGAAAGGGGAGAATGTATCTACCACTGAGGTGGAGGGCACACTCAGCCGCTGCTTCATATGGCAGATG
 TGGCAGTTTATGGTGTGAGGTGCCAGGAAGTGAAGGCCGAGCAGGAATGGCTGCCGTTGCAAGTCCCATCAGCACTGT
 GACCTGGAGAGCTTTGCACAGACCTTGAAAAAGGAGCTGCTCTGTATGCCCGCCCCATCTTCTGCGCTTCTTGCTGA
 GCTGCACAAGACAGGGGACCTTCAAGTTCAGAAAGACAGAGTTGCGGAAGGAGGGCTTTGACCCATCTGTTGTGAAGACC
 CGCTGTTCTATCTGGATGCTCGGAAGGGCTGCTACGTTGCACCTGGACCAAGGAGGCTTATACCCGATCCAGGCAGGCGAG
 GAGAAGCTGTGATTTCCCTTACATCCCTCTGAGGGCCAGAAGATGCTGATTACAGAGCCCTAGCGTCCACCCAGAGGG
 TCCTGGGCAATCCAGACCAAGCTAGCAGGGCTCCGACCTCCGCCCTAGGTGCTGATCTCCCTCTCCCAACTGCCA
 AGTGAAGCTCACTGCCGCTTCCCGACCTCCAGAGGCTTCTGTGAAGTCTCATCCAAGCTGTGTCTTCTGGTCCAGGCG
 TGGCCCCCTGGCCCCAGGGTTCTGATAGGCTCCTTTAGGATGGTATCTTGGGTCCAGCGGGCCAGGGTGTGGGAGAGGCA
 TCACTAAGATCCCTCCAATCAGAAGGGAGCTTACAAAGGAACCAAGGCCAAGCTGTAGACTCAGGAAGCTAAGTGGCCA
 GAGACTATAGTGGCCAGTCATCCCATGTCCACAGAGGATCTTGTCCAGAGCTGCCAAAGTGTACCTCTCCCTGCTCTG

ACCTCTGGGAAAGAGGACAGCATGTGGCCACTGGGCACCTGTCTCAAGAAGTCAGSATCACACACTCAGTCCTTGT
 CTCCAGGTTCCCTTGTCTTGTCTCGGGAGGGAGGGACGAGTGTCTGTCTGCTCTCTGCTGTCTGTGAGTCTGTG
 TTGCTTCTCCATCTGTCTAGCCTGAGTGTGGGTGGAACAGGCATGAGGAGAGTGTGGCTCAGGGGCCAATAAAGCTCTG
 CTTGACTCCTCTTAAAAA

Figure 43A

mmFATP4 protein sequence

MLLGASLVGALLFSKLVKLFWTOVGFSLLLLYLGS GGWR F IRVFIKTVRRDIFGGMVLLKVTKVRYLYOERKTVPLLF
 ASMVORHFDKLTALIFEGTDTHWTFROLDEYSSVANFLQARGLASGNVVALFMENRNEFVGLWLGMAXLGVAAALINTNL
 RRDALRHCLDTSKARALIFGSEMASAICEIHASLEPTLSLFCSGSWEPSVTPVSTEHLDPLLEDAFKHLPSPHDKGFTDK
 LFYIYTSGTGLPKAAIVVHSRYRMAASLVYVYGFMRPDDIVYDCLPLYHSRKHGRGDWQCLLHGMTVVIKFKFSASRFW
 DDCIKYNTVVQYIGELCRYLLNPPREAESRHKVRMALGNGLRQSIWTFSSRFHIPOVAEFYGAETECNCSLGNFDSRV
 GACGFNSRILSFVYPIRLVVRNEDTMELIRGPDGVICFQPGQPGOLVGRIIOQDPLRRFDGYLNOGANNKKIANDVFKK
 GDQAYLTGDLVMDLGYLYFRDRTGDTFRWKGENVSTTEVEGTLRLLHMDADVYGVVEVPFTEGRAGMAAVASPI S NC
 DLESFAQTLKKELPLYARPIFLRFLPELAKTGTFKFOKTELKKEGFDPSVVKDPLFYLDARKGCYVALDQEA YTRIQAGE
 EKL

Figure 43B

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hsFATP1 full lenght.DNA

10 20 30 40
TCGACCCACGGCGTCCGGGACCCCAAAGCAGAAGCCCGCA 40
CAGTAGGCACAGCGCACCCAAGAAGGGTCCAGGAGTCTGC 80
AGAAACAGAAAGGTCCCCGGCCTCAGCCTCCTAGTCCCTG 120
CCTGCCCTCCTGCCTGAGCTTCTGGGAGACTGAAGGCACGG 160
CTTGCAGCTTCAGGATGCGGGCTCCGGGTGCGGGCGCGGC 200
210 220 230 240
CTCGGTGGTCTCGCTGGCGCTGTTGTGGCTGCTGGGGCTG 240
CCGTGGACCTGGAGCGCGGCAGCGGCGCTCGGCGTGTACG 280
TGGGCAGCGGGCGGCTGGCGCTTCTCTGCGCATCGTCTGCAA 320
GACCGCGAGGCGAGACCTCTTCGGTCTCTCTGTGCTGATC 360
CGCGTGGCCTGGAGCTGCGGCGGCACCAGCGTGCCGGCC 400
410 420 430 440
ACACCATCCCGCGCATCTTTCAGGCGGTAGTGCAGCGACA 440
GCCCCGAGCGCCTGGCGCTGGTGGATGCCGGGACCGGCGAG 480
TGCTGGACCTTTGCGCAGCTGGACGCC TACTCCAATGCGG 520
TAGCCAACCTCTTCCGCCAGCTGGGCTTCGCGCCGGGCGA 560
CGTGGTGGCCATCTTCTTGGAGGGCGGCCGGAGTTCTGTG 600
610 620 630 640
GGGCTGTGGCTGGGCTGGGCAAGGCGGGCATGGAGGCCG 640
CGCTGCTCAACGTGAACCTGCGGCGCGAGCCCCCTGGCCTT 680
CTGCCTGGGCACCTCGGGCGCTAAGGCCCTGATCTTTGGA 720
GGAGAAATGGTGGCGGCGGTGGCCGAAGTGAGCGGGCATC 760
TGGGGAAAAGTTTGATCAAGTTCTGCTCTGGAGACTTTGG 800
810 820 830 840
GCCCCAGGGCATCTTGCCGGACACCCACCTCCTGGACCCG 840
CTGCTGAAGGAGGCC TCTACTGCCCCCTTGGCACAGATCC 880
CCAGCAAGGGCATGGACGATCGTCTTTTCTACATCTACAC 920
GTCCGGGACCACCGGGCTGCCCAAGGCTGCCATTGTCTGTG 960
CACAGCAGGTACTACCGCATGGCAGCCTTCGGCCACCACG 1000
1010 1020 1030 1040
CCTACCGCATGCAGGCGGCTGACGTGCTCTATGACTGCCT 1040
GCCCCGTGTACCACTCGGCAGGAAACATCATCGGCGTGGGG 1080
CAGTGTCTCATCTATGGGCTGACAGTCGTCTCCGCAAGA 1120
AATTCTCGGCCAGCCGCTTCTGGGACGACTGCATCAAGTA 1160
CAACTGCACGGTGGTTCAGTACATCGGGGAGATCTGCCGC 1200

Fig. 44A

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hsFATP1 full lenght.DNA

1210 1220 1230 1240
TACCTGCTGAAGCAGCCGGTGC GCGAGGCGGAGAGGCGAC 1240
ACCGCGTGC GCGCTGGCGGTGGGGAACGGGCTGCGTCTCTGC 1280
CATCTGGGAGGAGTTTACGGAGCGCTTCGGCGTACGCCAA 1320
ATCGGGGAGTTCTACGGCGCCACCGAGTGCAACTGCAGCA 1360
TTGCCAACATGGACGGCAAGGTTCGGCTCCTGTGGTTTCAA 1400
1410 1420 1430 1440
CAGCCGCATCCTGCCCCACGTGTACCCCATCCGGCTGGTG 1440
AAGGTCAATGAGGACACAATGGAGCTGCTGCGGGATGCC 1480
AGGGCCTCTGCATCCCTGCCAGGCCGGGGAGCCTGGCCT 1520
CCTTGTGGGTGAGATCAACCAACAGGACCCGCTGCGCCGC 1560
TTGATGGCTATGTCAGCGAGAGCGCCACCAGCAAGAAGA 1600
1610 1620 1630 1640
TCGCCCCACAGCGTCTTCAGCAAGGGCGACAGCGCCTACCT 1640
CTCAGGTGACGTGCTAGTGATGGATGAGCTGGGCTACATG 1680
TACTTCCGGGACCGTAGCGGGGACACCTTCCGCTGGCGAG 1720
GGGAGAACGTCTCCACCACCGAGGTGGAGGGCGTGCTGAG 1760
CCGCTGCTGGGCCAGACAGACGTGGCCGTCTATGGGGTG 1800
1810 1820 1830 1840
GCTGTTCAGGAGTGGAGGGTAAGGCAGGGATGGCGGCCG 1840
TCGCAGACCCCCACAGCCTGCTGGACCCCAACGCGATATA 1880
CCAGGAGCTGCAGAAGGTGCTGGCACCCCTATGCCCCGCC 1920
ATCTTCTGCGCCTCCTGCCCCAGGTGGACACCACAGGCA 1960
CCTTCAAGATCCAGAAGACGAGGCTGCAGCGAGAGGGCTT 2000
2010 2020 2030 2040
TGACCCACGCCAGACCTCAGACCGGCTCTTCTTCTGAC 2040
CTGAAGCAGGGCCACTACCTGCCCTTAAATGAGGCACTCT 2080
ACACTCGCATCTGCTCGGGCGCCTTCGCCCTCTGAAGCTG 2120
TTCCTCTACTGGCCACAACTCTGGGCCTGGTGGGAGAGG 2160
CCAGCTTGAGCCAGACAGCGCTGCCAGGGGTGGCCGCCT 2200
2210 2220 2230 2240
AGTACACACCCACCTGGCCGAGCTGTACCTGGCACGGCCC 2240
ATCCTGGACTGAGAACTGGAACCTCAGAGGAACCCGTGC 2280
CTCTCTGCTGCCTTGGTGCCCTGTGTCTGCCTCCTCTCC 2320
CTGCTTTTCAGCCTCTGTCTCCTTCCATCCCTGTCCCTGT 2360
CTGGCCTTAACTCTTCCCTCTCTTTCTTTCTTTCTTTCT 2400
2410 2420 2430 2440
TTCTTTTTTTTTAAGATAGAGTCTCACTCTGCTGCCCCGG 2440
CTAGAGTGCAGTGGTGGGATCTCGGCTCACTGCAACCTCT 2480
GCCTCCTGGGGTTCAAGTGATCCTCCACCTCAGCCTCCT 2520
GAGTAGCTGGGATTACAGGCACCCGCCACACGTCAGCT 2560
AATTTTATATTTTATAGTAGAGACGGGGTTTACCATGTT 2600

Fig. 44B

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hsFATP1 full lenght.DNA

```

      2610      2620      2630      2640
      | | | | | | | | | | | | | | | | | |
GGTCAGGCTGGTCTTGAACCTCCTGACCTCAGGTGATCCGC 2640
TGGCCTCGGCCTCCCAGAGTGCTGGGATTATAGCGGTGAG 2680
CCTCTGGCCCGGCCTTTCTTTTTCTCTCTCTCTCTGCC 2720
GAGAGTGAACACACGTGTCTCTGGGAGCTGCATCTTGTGT 2760
AGGGTCCAGCTGCTTTTGGGGACTGCAGGAATCATCTCCC 2800
      2810      2820      2830      2840
      | | | | | | | | | | | | | | | | | |
CTGGGCCCTGGACTCGGACTGGGGCCTCCCCACCTCCCTC 2840
TCGGCTGTGCCTTACGGAGCCCCAATCCAGGCCTCCTGTG 2880
GCTGTGGGTTCAGATGCTGCAGCTCCATGTGACTTCCA 2920
AGCAGGCCCTCCGCCCTCCCTGCTGAATGGAGGAGCCGGG 2960
GTCCCCCAGGCCAACTGGAAAATCTCCAGGCTAGGCCA 3000
      3010      3020      3030      3040
      | | | | | | | | | | | | | | | | | |
ATTGCCCTTTTGCACTTCCCCGTTCTGTGACATTTCCCA 3040
GCCCCACCTTCCCCCTCTGATGCCCTGAAAGCTTCCGGAA 3080
TTGACTGTGACCACCTGGATGTCACCACTGTCAGCCCCCTG 3120
CCTTGATGTCCCCATTTAGCCATCTCCATGGAGCTCCTGC 3160
TGGAGGGCCCTGAACCTGCACTGCGTGGCTGCCAGCCA 3200
      3210      3220      3230      3240
      | | | | | | | | | | | | | | | | | |
GCTGCCTCCTGTCTCTGGGAGGAGGCCTCCTGGGTGTCTC 3240
ATCTGGTGTGTCTACTGGAGGGTCCCACAGGAGAGGCAGC 3280
AGAGGGGTGAGGGGAGGTCTCTGCCGGGGGTGGCCTCT 3320
CAAGCCTCAGGGGTTCTAGCCTGTTGAATATACCCACCT 3360
GGTGGGTGGCCCTCCGATGTCCCCACTGATGGCTCTGAC 3400
      3410      3420      3430      3440
      | | | | | | | | | | | | | | | | | |
ACCGTGTGGTGGCGATGTCCCAGACAATCCCACCAGGAC 3440
GGCCCAGACATCCCTACTGGCTTCGCTGGTGGCTCATCTC 3480
GAACATCCACGCCAGCCTTTCTGGGGCCGGCCACCCAGGC 3520
CGCCTGTCCGTCTGTCTCCCTCCAGCAGCACCCCTGGC 3560
CCCTGGAGTGGTGGGGCCATGGCAAGAGACACCGTGGCGT 3600
      3610      3620      3630      3640
      | | | | | | | | | | | | | | | | | |
CTCATGTGAACCTTCTCTGGGCACTGTGGTTTTATTCCTA 3640
ATTGATTTAAGAAATAAACCTGAAGACCGTCTGGTGAAAA 3680
AAAAAAAAAAAAA 3694

```

Fig. 44C

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hsFATP1 full length.protein

10 20 30 40
MRAPGAGAASVVSLALLWLLGLPWTWSAAAAALGVYVSGG 40
WRFLRIVCKTARRDLFGLSVLIRVRLELRRHORAGHTIPR 80
IFOAVVOROPERLALVDAGTGECWTFALDAYSNAVANLF 120
ROLGFAPGDVVAIFLEGRPEFVGLWLGLAKAGMEAALLNV 160
NLRREPLAFCLGTSGAKALIFGGEMVAAYAEVSGHLGKSL 200
210 220 230 240
IKFCSGDLGPEGILPDTHLLDPLLKEASTAPLAQIPSKGM 240
DDRLFYIYTS GTTGLPKAAIVVHSRYRMAAFGHHAYRMO 280
AADVLYDCLPLYHSAGNIIGVGOCLIIYGLTVVLRKKFSAS 320
RFWDDCIKYNCTVVQYIGEICRYLLKOPVREAERRHRVRL 360
AVGNGLRPAIWEETERFGVROI GEFYGATECNCSIANMD 400
410 420 430 440
GKVGSCGFNSRILPHVYPIRLVKVNEDTMELLRDAOGLCI 440
PCOAGEPGLLVGOINOODPLRRFDGYVSESATSKKIAHSV 480
FSKGDSAYLSGDVLMDELGYMYFRDRSGDTFRWRGENVS 520
TTEVEGVLSRLLGOTDVAVYGVAVPGVEGKAGMAAVADPH 560
SLDPNAIYOELOKVLAPYARPIFLRLLPQVDITGTFKIO 600
610 620 630 640
KTRLREGFDPROTSORLFFLDLKOGHYLPLNEAVYTRIC 640
SGAFAL. 647

Fig. 45

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hsVLACS full lenght.DNA

10 20 30 40
GGAATTCCAAAAAAAAAATACGACTACACCTGCTCCGG 40
AGCCCGCGGCGGTACCTGCAGCGGAGGAGCTCTGTCTTCC 80
CCTTCATCTCAGCGAGCCCGGCGTCCCGCCGCGTGC GCC 120
CCGGCGCAGCCCGCCAGTCCGCCCGGAGCCCGCCAGTCG 160
CCGCGCTGCACGCCCGGGGTGAACCTCTGCCCTCGCTGG 200
210 220 230 240
GACAGAGGGCCCCGCAGCCGTCATGCTTTCCGCCATCTAC 240
ACAGTCCTGGCGGGACTGCTGTTCTTCCGCTCCTGGTGA 280
ACCTCTGCTGCCCATACTTCTTCCAGGACATAGGCTACTT 320
CTTGAAGGTGGCCGCCGTGGGCCGGAGGGTGC GCAGCTAC 360
GGGACGCGCGCGCGCGCACCATCTGCGGGCGTTCC 400
410 420 430 440
TGGAGAAAGCGCGCCAGACGCCACACAAGCCTTTTCTGCT 440
CTTCCGCGACGAGACTCTCACCTACGCGCAGGTGGACCGG 480
CGCAGCAATCAAGTGGCCCGGGCGCTGCACGACCACCTCG 520
GCCTGCGCCAGGAGACTGCGTGGCGCTCCTTATGGGTAA 560
CGAGCCGGCTACGTGTGGCTGTGGCTGGGGCTGGTGAAG 600
610 620 630 640
CTGGGCTGTGCCATGGCGTGCCTCAATTACAACATCCGCG 640
CGAAGTCCCTGCTGCACTGCTTCCAGTGCTGCGGGGCGAA 680
GGTGTCTGCTGGTGTGCCAGAACTACAAGCAGCTGTGCGAA 720
GAGATACTGCCAAGCCTTAAAAAAGATGATGTGTCCATCT 760
ATTATGTGAGCAGAACTTCTAACACAGATGGGATTGACTC 800
810 820 830 840
TTTCCTGGACAAAGTGGATGAAGTATCAACTGAACCTATC 840
CCAGAGTCATGGAGGTCTGAAGTCACTTTTCCACTCCTG 880
CCTTATACATTTATACTTCTGGAACACAGGTCTTCCAAA 920
AGCAGCCATGATCACTCATCAGCGCATATGGTATGGAAC 960
GGCCTCACTTTTGTAAAGCGGATTGAAGGCAGATGATGTCA 1000
1010 1020 1030 1040
TCTATATCACTCTGCCCTTTTACCACAGTGCTGCACTACT 1040
GATTGGCATTCACGGATGTATTGTGGCTGGTGCTACTCTT 1080
GCCTTGC GGACTAAATTTTTCAGCCAGCCAGTTTGGGATG 1120
ACTGCAGAAAAATACAACGTCACTGTCAATTCAGTATATCGG 1160
TGAAC TGCTTCGGTATTTATGCAACTCACCACAGAAACCA 1200

Fig. 46 A

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hsVLACS full lenght.DNA

1210 1220 1230 1240
AATGACCGTGATCATAAAGTGAGACTGGCACTGGGAAATG 1240
GCTTACGAGGAGATGTGTGGAGACAATTTGTCAAGAGATT 1280
TGGGGACATATGCATCTATGAGTTCTATGCTGCCACTGAA 1320
GGCAATATTGGATTTATGAATTATGCGAGAAAAGTTGGTG 1360
CTGTTGGAAGAGTAAACTACCTACAGAAAAAAATCATAAC 1400
1410 1420 1430 1440
TTATGACCTGATTAAATATGATGTGGAGAAAGATGAACCT 1440
GTCCGAGATGAAAAATGGATATTGCGTCAGAGTTCCCAAAG 1480
GTGAAGTTGGACTTCTGGTTTGCAAAATCACACAACCTTAC 1520
ACCATTTAATGGCTATGCTGGAGCAAAGGCTCAGACAGAG 1560
AAGAAAAAACTGAGAGATGTCTTTAAGAAAGGAGACCTCT 1600
1610 1620 1630 1640
ATTTCAACAGTGGAGATCTCTTAATGGTTGACCATGAAAA 1640
TTTCATCTATTTCCACGACAGAGTTGGAGATACATTCCGG 1680
TGGAAGGGGAAAAATGTGGCCACCACTGAAGTTGCTGATA 1720
CAGTTGGACTGGTTGATTTTGTCCAAGAAGTAAATGTTTA 1760
TGGAGTGCATGTGCCAGATCATGAGGGTCGCATTGGCATG 1800
1810 1820 1830 1840
GCCTCCATCAAAATGAAAGAAAACCATGAATTTGATGGAA 1840
AGAAACTCTTTTCAGCACATTGCTGATTACCTACCTAGTTA 1880
TGCAAGGCCCCGGTTTCTAAGAATACAGGACACCAATTGAG 1920
ATCACTGGAACTTTTTAAACACCGCAAAATGACCCTGGTGG 1960
AGGAGGGCTTTAACCCTGCTGTTCATCAAAGATGCCTTGTA 2000
2010 2020 2030 2040
TTTCTTGGATGACACAGCAAAAATGTATGTGCCTATGACT 2040
GAGGACATCTATAATGCCATAAGTGCTAAAACCCTGAAAC 2080
TCTGAATATTTCCAGGAGGATAACTCAACATTTCCAGAAA 2120
GAAACTGAATGGACAGCCACTTGATATAATCCAACTTTAA 2160
TTTGATTGAAGATTGTGAGGAAATTTGTAGGAAATTTGC 2200
2210 2220 2230 2240
ATACCCGTAAAGGGAGACTTTTTTAAATAACAGTTGAGTC 2240
TTTGCAAGTAAAAAGATTTAGAGATTATTATTTTTCAGTG 2280
TGCACCTACTGTTTGTATTTGCAAACTGAGCTTGTGGAG 2320
GGAAGGCATTATTTTTTAAATACTTAGTAAATTAAATGA 2360
AC 2362

Fig. 46B

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hsVLACS full lenght.protein

10 20 30 40
MLSAITYVLAGLLFLPLL VNLCCPYFFODIGYFLKVAAVG 40
RRVRSYGORRPARTILRAFLEKAROTPHKPFLLFRDETLT 80
YAQVDRRSNOVARALHHLGLROGDCVALLMGNEPAYVWL 120
WLGLVKLGCAMACLNYNIRAKSLLHCFCCGAKVLLVSPE 160
LOAAVEEILPSLKKDDVSIYYVSRTSNTDGI DSFLDKVDE 200
210 220 230 240
VSTEPIPESWRSEVTFSTPALYIYTS GTTGLPKAAMITHO 240
RIWYGTGLTFVSGLKADDVIYITLPFYHSAALLIGIHGCI 280
VAGATLALRTKFSASOFWDDCRKYNVTVIQYIGELLRYLC 320
NSPOKPNDRDHKVRLLALGNGLRGDVWROFVKRFGDICIYE 360
FYAATEGNIGFMNYARKVGAVGRVNYLQKKIITYDLIKYD 400
410 420 430 440
VEKDEPVRDENGVCVRVPKGEVGLLVCKITOLTPFN GYAG 440
AKAOTEKKKL RDVFKKGDLYFNSGDLLMVDHENFIYFHDR 480
VGDTFRWKGENVATTEVADTVGLVDFVQEVNVYGVHVPDH 520
EGRIGMASIKMKENHEFDGKKLFQHIADYLPSYARPRFLR 560
IODTIEITGTFKHKRMTLVEEGFNPAVIKDALYFLDDTAK 600
610 620 630 640
MYVPMTEDIYNAISAKTLKL. 621

Fig. 47

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hsFATP3 partial.DNA

10 20 30 40
AAGTTCTCGGCTGGTCAGTTCTGGGAAGATTGCCAGCAGC 40
ACAGGGTGACGGTGTTCAGTACATTGGGGAGCTGTGCCG 80
ATACCTTGTCACCAGCCCCGAGCAAGGCAGAACGTGGC 120
CATAAGGTCCGGCTGGCAGTGGGCAGCGGGCTGCGCCCAG 160
ATACCTGGGAGCGTTTTGTGCGGCGCTTCGGGCCCCCTGCA 200
210 220 230 240
GGTGCTGGAGACATATGGACTGACAGAGGGCAACGTGGCC 240
ACCATCAACTACACAGGACAGCGGGGCGCTGTGGGGCGTG 280
CTTCCTGGCTTTACAAGCATATCTTCCCCCTTCTCCTTGAT 320
TCGCTATGATGTCAACACAGGAGAGCCAATTGCGGACCCC 360
CAGGGGCACGTGATGGCCACATCTCCAGGTGAGCCAGGGC 400
410 420 430 440
TGCTGGTGGCCCCGGTAAGCCAGCAGTCCCCATTCTGGG 440
CTATGCTGCCGGGCCAGAGCTGGCCCCAGGGGAAGTTGCTA 480
AAGGATGTCTTCCGGCCTGGGGATGTTTTCTTCAACTG 520
GGGACCTGCTGGTCTGCGATGACCAAGGTTTTCTCCGCTT 560
CCATGATCGTACTGGAGACACCTTCAGGTGGAAGGGGAG 600
610 620 630 640
AATGTGGCCACAACCGAGGTGGCAGAGGTCTTCGAGGCCC 640
TAGATTTTCTTCAGGAGGTGAACGTCTATGGAGTCACTGT 680
GCCAGGGCATGAAGGCAGGGCTGGAATGGCAGCCCTAGTT 720
CTGCGTCCCCCCCCACGCTTTGGACCTTATGCAGCTCTACA 760
CCCACGTGTCTGAGAACTTGCCACCTTATGCCCGGCCCCG 800
810 820 830 840
ATTCCTCAGGCTCCAGGAGTCTTTGGCCACCACAGAGACC 840
TTCAAACAGCAGAAAGTTCGGATGGCAAATGAGGGCTTCG 880
ACCCAGCACCCCTGTCTGACCCACTGTACGTTCTGGACCA 920
GGCTGTAGGTGCCTACCTGCCCCTCACAACTGCCCCGGTAC 960
AGCGCCCTCCTGGCAGGAAACCTTCGAATCTGAGAACTTC 1000
1010 1020 1030 1040
CACACCTGAGGCACCTGAGAGAGGAACTCTGTGGGTGGG 1040
GGCCGTTGCAGGTGTACTGGCTGTCAGGGATCTTTTCTA 1080
TACCAGAACTGCGGTCACTATTTTGTAAATAATGTGGCTG 1120
GAGCTGATCCAGCTGTCTCTGACAAAAAATAAATAAATAA 1160
AAAGGGCGGGCCG 1173

Fig. 48

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hsFATP3partial.protein

10 20 30 40
KFSAGQFWEDCOOHRVTVFQYIGELCRYLVNPPSKAERG 40
HKVRLAVGSGLRPDWVERFVRRFGPLOVLETYGLTEGNVA 80
TINYTGORGAVGRASWLYKHIFPFSLIRYDVTTGEPIRD 120
OGHCMATSPGEPGLLVAPVSQOSPFLGYAGGPFLAOGKLL 160
KDVFRPGDVFFNTGOLLVCDDOGFLRFHDRTGDTFRWKGE 200
210 220 230 240
NVATTEVAEVFEALDFLOEVNVYGVTVPGHEGRAGMAALV 240
LRPPHALDLMOLYTHVSENLPYARPRFLRLOESLATTET 280
FKQOKVRMANEGFDPSTLSDFLYVLDOAVGAYLPLTTARY 320
SALLAGNLR I. 331

Fig. 49

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hsFATP4 full length

10 20 30 40
CGACCCACGCGTCCGGGCGGGCGGGCGGGCGGGCGGGCGG 40
GGGCTGGCGGGGCGGGCGGGCCATGCAGGGCGCAGAGCCG 80
GCTAAACCCCTGCTGAGACCCGGCTCCGTGCGTCCAGGGGC 120
GGCTAATGCCCCCTACGCTGTCTACGCTGCTGCAACCGGG 160
CCGCATCTGGACGGGGCGCCGCGCGCGGAGCCGACGCCG 200

210 220 230 240
GGCCACAATGCTGCTTGGAGCCTCTCTGGTGGGGGTGCTG 240
CTGTTCTCCAAGCTGGTGTGAACTGCCCTGGACCCAGG 280
TGGGATTCTCCCTGTGTCTCTACTTGGGATCTGGCGG 320
CTGGCGCTTCATCCGGGTCTTCATCAAGACCATCAGGCGC 360
GATATCTTTGGCGGCTGGTCCTCCTGAAGGTGAAGGCAA 400

410 420 430 440
AGGTGCGACAGTGCCTGCAGGAGCGGCGGACAGTGCCTAT 440
TTTGTCTTGCCTCTACCGTTCGGCGCCACCCCGACAAGACG 480
GCCCTGATCTTCGAGGGCACAGATACCCACTGGACCTTCC 520
GCCAGCTGGATGAGTACTCAAGCAGTGTAGCCAACCTTCT 560
GCAGGCCCGGGGCTGGCCTCGGGCGATGTGGCTGCCATC 600

610 620 630 640
TTCATGGAGAACCGCAATGAGTTTCGTGGGCCTATGGCTGG 640
GCATGGCCAAGCTCGGTGTGGAGGCAGCCCTCATCAACAC 680
CAACCTGCGGCGGGATGCTCTGCTCCACTGCCTCACCACC 720
TCGCGCGCACGGGCCCTTGTCTTTGGCAGCGAAATGGCCT 760
CAGCCATCTGTGAGGTCCATGCCAGCCTGGACCCCTCGCT 800

810 820 830 840
CAGCCTCTTCTGCTCTGGCTCCTGGGAGCCCGGTGCGGTG 840
CCTCCAAGCACAGAACACCTGGACCTCTGCTGAAAGATG 880
CTCCCAAGCACCTTCCCAGTTGCCCTGACAAGGGCTTAC 920
AGATAAACTGTTCTACATCTACACATCCGGCACCACAGGG 960
CTGCCCCAAGGCCCATCGTGGTGCACAGCAGGTATTACC 1000

1010 1020 1030 1040
GCATGGCTGCCCTGGTGTACTATGGATTCCGCATGCGGCC 1040
CAACGACATCGTCTATGACTGCCTCCCCCTCTACCACTCA 1080
GCAGGAAACATCGTGGGAATCGGCCAGTGCCTGCTGCATG 1120
GCATGACGGTGGTGAATCGGAAGAAGTTCTCAGCCTCCCG 1160
GTTCTGGGACGATTGTATCAAGTACAACCTGCACGATTGTG 1200

Fig. 50A

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hsFATP4 full length

1210 1220 1230 1240
CAGTACATTGGTGAACGTGTGCCGCTACCTCCTGAACCAGC 1240
CACC GCGGGAGGCAGAAAACCAAGCACCAGGTTCGCATGGC 1280
ACTAGGCAATGGCTCCGGCAGTCCATCTGGACCAACTTT 1320
TCCAGCCGCTTCCACATACCCAGGTGGCTGAGTTCTACG 1360
GGGCCACAGAGTGCAACTGTAGCCTGGGCAACTTCGACAG 1400

1410 1420 1430 1440
CCAGGTGGGGGCTGTGGTTTCAATAGCCGCATCCTGTCC 1440
TTCGTGTACCCATCCGGTTGGTACGTGTCAACGAGGACA 1480
CCATGGAGCTGATCCGGGGGCCCCGACGGCGTCTGCATTCC 1520
CTGCCAGCCAGGTGAGCCGGGCCAGCTGGTGGGCCGCATC 1560
ATCCAGAAAGACCCCTGCGCCGCTTCGATGGCTACCTCA 1600

1610 1620 1630 1640
ACCAGGGCGCCAACAACAAGAAGATTGCCAAGGATGTCTT 1640
CAAGAAGGGGGACCAAGGCTTACCTTACTGGTGATGTGCTG 1680
GTGATGGACGAGCTGGGCTACCTGTACTTCCGAGACCGCA 1720
CTGGGGACACGTTCGGCTGGAAAGGTGAGAACGTGTCCAC 1760
CACC GAGGTGGAAGGCACACTCAGCCGCTGCTGGACATG 1800

1810 1820 1830 1840
GCTGACGTGGCCGTGTATGGTGTGAGGTGCCAGGAACCG 1840
AGGGCCGGGCGGAATGGCTGCTGTGGCCAGCCCCACTGG 1880
CAACTGTGACCTGGAGCGCTTTGCTCAGGTCTTGGAGAAG 1920
GAACTGCCCTGTATGCGCGCCCCATCTTCCTGCGCCTCC 1960
TGCTTGAGCTGCACAAAACAGGAACCTACAAGTTCCAGAA 2000

2010 2020 2030 2040
GACAGAGCTACGGAAGGAGGGCTTTGACCCGGCTATTGTG 2040
AAAGACCCGCTGTTCTATCTAGATGCCCAGAAGGGCCGCT 2080
ACGTCCCGCTGGACCAAGAGGCTTACAGCCGCATCCAGGC 2120
AGGCGAGGAGAAGCTGTGATTCCCCCATCCCTCTGAGGG 2160
CCGGCGGATGCTGGATCCGGAGCCCCAGGTTCCGCCCCAG 2200

2210 2220 2230 2240
AGCGGTCCTGGACAAGGCCAGACCAAGCAAGCAGGGCCT 2240
GGCACCTCCATCCTGAGGTGCTGCCCCCTCCATCCAAACT 2280
GCCAAGTGACTCATTTGCCTTCCCCAACCTTCCAGAGGCTT 2320
TCTGTGAAAGTCTCATGTCCAAGTTCGGTCTTCTGGGCTG 2360
GGCAGGCCCTCTGGTTCCCAGGCTGAGACTGACGGGTTTT 2400

2410 2420 2430 2440
CTCAGGATGATGTCTTGGGTGAGGCTAGGGAGAGGACAAG 2440
GGGTACCGAGCCCCTCCAGAGAGCAGGGAGCTTATAAA 2480
TGGAACCAGAGCAGAAGTCCCCAGACTCAGGAAGTCAACA 2520
GAGTGGGCAGGGACAGTGGTAGCATCCATCTGGTGGCCAA 2560
AGAGAATCGTAGCCCCAGAGCTGCCCAAGTTCCTGAGGCT 2600

Fig. 50B

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hsFATP4 full length

2610 2620 2630 2640

CCACCCCCACCTCCAGGAGGGGAGGAGGACCTGACATC 2640
TGTAGGTGGCCCTGATGCCCCATCTACAGCAGGAGGTCA 2680
GGACCACGCCCCTGGCCTCTCCCCACTCCCCCATCCTCCT 2720
CCCTGGGTGGCTGCCTGATTATCCCTCAGGCAGGGCCTCT 2760
CAGTCCTTGTGGGTCTGTGTCACCTCCATCTCAGTCTTGG 2800

2810 2820 2830 2840

CCTGGCTATGAGGGGAGGAGGAATGGGAGAGGGGGCTCAG 2840
GGGCCAATAAACTCTGCCTTGAGTCCTCCTAAAAAAAAAA 2880
AAAAAAAAAAAAAAAAAAAAAAAAAAAA 2907

Fig. 50C

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hsFATP4 full length. protein

10 20 30 40
MLLGASL¹GVLLFSKLVLKLPWTVGFSLFLYLGGGWR 40
FIRVFIKTIRRDIFGGLVLLKVKAKVROCLQERRTPILF 80
ASTVRRHPDKTALIFEGTDTHWTFROLDYSSSVANFLOA 120
RGLASGDVAAIFMENRNEFVGLWLGMAKLGVEAALINTNL 160
RRDALLHCLTTSRARALVFGSEMASAICEVHASLOPSLSL 200

210 220 230 240
FCSGSWEPGAAPPSTEHLDPLLKDAPKHLPSDFKGFDTK 240
LFYIYTSGLTGLPKAAIVVHSRYRMAALVYGFMRPND 280
IVYDCLPLYHSAGNIVGIGOCLLHGMTVVIRKKFSASRFW 320
DDCIKYNCTIVQYIGELCRYLLNOPPREAENOHVORMALG 360
NGLROSIWTFNFSRFHIPOVAEFYGATECNCNLGNFDSOV 400

410 420 430 440
GACGFNSRILSFVYPIRLVRVNEDTMELIRGPDGVCIPCO 440
PGEPLGVGRILQKDPLERRFDGYLNOGANNKKIAKDVFKK 480
GDOAYLTGDVLMDELGYLYFRDRTGDTFRWKGENVSTTE 520
VEGTLSRLLDMADVAVYGVEVPGTEGRAGMAAVASPTGNC 560
DLERFAQVLEKELPLYARPIFLRLLPELHKTGTYKFOKTE 600

610 620 630 640
LRKEGFDPAIVKDPFLYLDQKGRYVPLDQEAYSRIQAGE 640
EKL 643

Fig. 51

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>hsFATP5(partial)

GTCGTTGGGATCCTCGGCTGCTTAGATCTCGGAGCCACCTGTGTTCTGGCCCCCAAG
TTCTCTACTTCCTGCTTCTGGGA
TGACTGTCGGCAGCATGGCGTGACAGTGATCCTGTATGTGGGCGAGCTCCTGCGATA
CTTGTAACATTCCCCAGCAAC
CAGAGGACCGGACACATACAGTCCGCCTGGCAATGGGCAATGGACTACGGGCTGAT
GTGTGGGGAGACCTTCCAGCAGCG
TTTCGGTCCTATTTCCGATCTNGGGAAGTCTTACGGGCTTCCACAGAAGGGCAACAT
GGGGCTTTAGTTCAAATATTGTT
GGGGGCGCTGCGGGGCCCTGGGGGCAAAGATGGAGCTTGCCTCCTCCGAATGCTGT
CCCCCTTTGAGCTGGTGCAGTTCG
ACATGGAGGCGGCGGAGCCTGTGAGGGACAATCAGGGCTTCTGCATCCCTGTAGGG
CTAGGGGAGCCGGGGCTGCTGTTG
ACCAAGGTGGTAAGCCAGCAACCCTTCGTGGGCTACCGCGGCCCCCGAGAGCTGTC
GGAACGGAAGCTGGTGCACACGT
GCGGCAATCGGGCGACGTTTACTACAACACCGGGGACGTAAGGCCATGGACCGCG
AAGGCTTCCTCTACTTCCGCGACC
GACTCGGGGACACCTTCCGATGGAAGGGCGAGAACGTGTCCACGCACGAGGTGGAG
GGCGTGTTGTCGAGGTGGACTTC
TTGCAACAGGTTAACGTGTATGGCGTGTGCGTGCCAGGTTGTGAGGGTAAGGTGGGC
ATGGCTGCTGTGGCATTAGCCCC
CGGCCAGACTTTGACGGGGAGAAGTTGTACCAGCACGTTTCGCGCTTGGCTCCCTGC
CTACGCTACCCCCCATTTATCC
GCATCCAGGACGCCATGGAGGTCACCAGCACGTTCAAACCTGATGAAGACCCGGTTG
GTGCGTGAGGGCTTCAATGTGGGG
ATCGTGGTTGACCCTCTGTTTGTACTGGACAACCGGGCCAGTCCTTCCGGCCCCCTG
ACGGCAGAAATGTACCAGGCTGT
GTGTGAGGGAACCTGGAGGCTCTGATCACCTGGCCAACCCACTGGGGTAGGGATCA
AAGCCAGCCACCCCCACCCCAACA
CACTCGGTGTCCCTTTATCCTGGGCCTGTGTGAATCCCAGCCTGGCCATACCTCA
ACCTCAGTGGGCTGGAAATGACA
GTGGGCCCTGTAGCAGTGGCAGAATAAACTCAGMTGYGTTACAGAAA

Fig. 52

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hsFATP5partial.protein

10 20 30 40
VVGILGCLDLGATCYLAPKFSTSCFWDDCRHGVTVILYV 40
GELLRYLCNIPOOPEDRTHTVRLAMGNGLRADVWGDLPA 80
FRSYFGSXEVLRASTEGOHGALVOILLGALRGPGGKDGAC 120
LLRMLSPFELVQFDMEEAEPVRDNOGFCIPVGLGEPGLLL 160
TKVVSQQPFVGYRGPRELSERKLVRNVROSGDVYYNTGOV 200
210 220 230 240
LAMDREGFLYFRDRLGDTFRWKGENVSTHEVEGVLSQVDF 240
LOQVNVYGVCPGCEGKVGMAAVALAPGOTFDGEKLYOHV 280
RAWLPAYATPHFIRIODAMEVTSTFKLMKTRLVREGFNVG 320
IVVDPLFVLONRAQSFRPLTAEMYQAVCEGTWRL 354

Fig. 53

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hsFATP6 full lenght.DNA

10 20 30 40
AACGGCAAGTAAGCGCAACGCAATTAATGTGAGTAGCTCA 40
CTCATTAGGCACCCAGGCTTTACACTTTATGCTTCCGGG 80
CTCGTATGTTGTGTGGAATTGTGAGCGGATACCAATTICA 120
CACAGGAACCGCTATGACATGATTACGAATTTAATACGA 160
CTCACTATAGGGAATTTGGCCCTCGAGGCCAAGAATTCGG 200
210 220 230 240
CACGAGGGGTGCTGAGCCCCTGCGCGGTTTCTGGTGCGTA 240
GAGACTGTAAATCGCTGCGCTTCTCAGTCATCATCATCCC 280
AGCTTTTCCCGGCTCGAATTCAGCCTCCAACCTCAAGCTCG 320
CGGGAAAGACTACCTGAGAGGAGAAAAGCTTCTGTCCCTG 360
GACCTTCTTCTGAGGGTGGAGTCGGAGGCTCCCTGCTTTC 400
410 420 430 440
CAGCCGCCCAGTGACCCAAGCTTAATCTTCAGCACCACTT 440
GGGGCGACCTTTTCGGTGCAAACCTACGATTCTGTTTCTC 480
AGGATTCTCTCCCATCCCGCTTCGCCCCGAAAAGCTGAC 520
AAGAACCTCAGGTGTAAGCCCTGAGTAGTGAGGATCTGCG 560
GTCTCCGTGGAGAGCTGTGCCTGGAAGAGAAGGACGCTGG 600
610 620 630 640
TGGGGGCTGAGATCAGAGCTGTCTTCTGGCCAGTTGCC 640
CCATGCTTCTGTCTATGGCTAACAGTTCTAGGGGCTGGAAT 680
GGTCGTCTGCACTTCTTGCAAACTCCTGTTCCCTTAC 720
TTTTGGGATGACTTCTGGTTCGTGTTGAAGGTGGTGCTCA 760
TTATAATTCGGCTGAAGAAGTATGAAAAGAGAGGGGAGCT 800
810 820 830 840
GGTGACTGTGCTGGATAAATTCTTGAGTCATGCCAAAAGA 840
CAACCTCGGAAACCTTTTCATCATCTATGAGGGAGACATCT 880
ACACCTATCAGGATGTAGACAAAAGGAGCAGCAGAGTGGC 920
CCATGCTTCTTGAACCAATTCCTCTCTGAAAAAGGGGGAC 960
ACGGTGGCTCTGCTGATGAGCAATGAGCCGGAATTCGTTT 1000
1010 1020 1030 1040
ACGTGTGGTTTCGGCCTCGCCAAGCTGGGCTGCGTGGTGGC 1040
CTTTCTCAACACCAACATTCGCTCCAACCTCCCTCCTGAAT 1080
TGCATCCGCGCCTGTGGGCCAGAGCCCTAGTGGTGGGCG 1120
CAGATTTGCTTGAACGGTAGAAGAAATCCTTCCAAGCCT 1160
CTCAGAAAAATATCAGTGTTTGGGGGATGAAAGATTCTGTT 1200

Fig. 54A

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hsFATP6 full lenght.DNA

```
1210      1220      1230      1240
.....
CCACAAGGTGTAATTTCACTCAAAGAAAACTGAGCACCT 1240
CACCTGATGAGCCCGTGCCACGCAGCCACCATGTTGTCTC 1280
ACTCCTCAAGTCTACTTGTCTTTACATTTTACCCTCTGGA 1320
ACAACAGGTCTACCAAAAGCAGCTGTGATTAGTCAGCTGC 1360
AGGTTTTAAGGGGTCTGTCTGTCTGTGGGCTTTTGGTTG 1400

1410      1420      1430      1440
.....
TACTGCTCATGACATTGTTTATATAACCTTTCCTCTGTAT 1440
CATAGTTCAGCAGCTATCCTGGGAATTTCTGGATGTGTTG 1480
AGTTGGGTGCCACTTGTGTGTTAAAGAAGAAATTTTCAGC 1520
AAGCCAGTTTTGGAGTGACTGCAAGAAGTATGATGTGACT 1560
GTGTTTCAGTATATTGGAGAAGTTTGTCTGCTACCTTTGCA 1600

1610      1620      1630      1640
.....
AACAATCTAAGAGAGAAGGAGAAAAAGGATCATAAGGTGCG 1640
TTTGGCAATTGGAAATGGCATACGGAGTGATGTATGGAGA 1680
GAATTTTACAGCAGATTTGGAAATATAAAGGTGTGTGAAC 1720
TTTATGCAGCTACCGAATCAAGCATATCTTTCATGAACATA 1760
CACTGGGAGAATTGGAGCAATTGGGAGAACAAATTTGTTT 1800

1810      1820      1830      1840
.....
TACAAACTTCTTTCCACTTTTGAAGTAAAGTATGACT 1840
TTCAGAAAGATGAACCCATGAGAAATGAGCAGGGTTGGTG 1880
TATTCATGTGAAAAAAGGAGAACCTGGACTTCTCATTCT 1920
CGAGTGAATGCAAAAAATCCCTTCTTTGGCTATGCTGGGC 1960
CTTATAAGCACACAAAAGACAAATTGCTTTGTGATGTTTT 2000

2010      2020      2030      2040
.....
TAAGAAGGGAGATGTTTACCTTAATACTGGAGACTTAATA 2040
GTCCAGGATCAGGACAATTTCCCTTTATTTTGGGACCGTA 2080
CTGGAGACACTTTCAGATGGAAAGGAGAAAATGTCGCAAC 2120
CACTGAGGTGCTGATGTTATTGGAATGTTGGATTTTATA 2160
CAGGAAGCAAACGTCTATGGTGTGGCTATATCAGGTTATG 2200

2210      2220      2230      2240
.....
AAGGAAGAGCAGGAATGGCTTCTATTATTTTAAAACCAAA 2240
TACATCTTTAGATTTGGAAAAAGTTTATGAACAAGTTGTA 2280
ACATTTCTACCAGCTTATGCTTGTCCACGATTTTAAAGAA 2320
TTCAGGAAAAAATGGAAGCAACAGGAACATTCAAACATT 2360
GAAGCATCAGTTGGTGAAGATGGATTTAATCCACTGAAA 2400

2410      2420      2430      2440
.....
ATTTCTGAACCACTTTACTTTCATGGATAACTTGAAAAAGT 2440
CTTATGTTCTACTGACCAGGGAAGTTTATGATCAAATAAT 2480
GTTAGGGGAAATAAACTTTAAGATTTTTATATCTAGAAC 2520
TTTCATATGCTTTCTTAGGAAGAGTGAGAGGGGGGTATAT 2560
GATTCITTTATGAAATGGGGAAAGGGAGCTAACATTAATTA 2600
```

Fig. 54B

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hsFATP6 full lenght.DNA

2610	2620	2630	2640
TGCATGTACTATATTTTCCTTAATATGAGAGATAATTTTTT	2640		
AATTGCATAAGAATTTTAATTTCTTTTAATTGATATAAAC	2680		
ATTAGTTGATTATTCCTTTTATCTATTTGGAGATTCAGTG	2720		
CATAACTAAGTATTTTCCTTAATACTAAAGATTTTAAATA	2760		
ATAAATAGTGGCTAGCGGTTTGGACAATCACTAAAAATGT	2800		
2810	2820	2830	2840
ACTTTCTAATAAGTAAAATTTCTAATTTTGAATAAAAGAT	2840		
TAAATTTTACTGAAAAAAAAAAAAAAAAAAAAAAAAATTGGCG	2880		
GCCGC	2885		

Fig. 54C

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hsFATP6 full lenght.protein

10 20 30 40
MLLSWLTIVLGAGMVVLHFLQKLLFPYFWDDFWVLKVVLI 40
IIRLKKEYEKGELVTVLQKFLSHAKROPRKPFIIYEGDIY 80
TYODVDKRSSRVAVHVLNHSSLKKGDTVALLMSNEPDFVH 120
VWFGGLAKLGCVVAFLENTNIRSNLLNCIRACGPRALVVG 160
DLLGTVEEILPSLSENI SVWGMKDSVPOGVISLKEKLST 200
210 220 230 240
PDEPVPRSHHVVSLLKSTCLYIFTSGTTGLPKAAVISQLO 240
VLRGSAVLWAFGCTAHDIVYITLPLYHSSAAILGISGCVE 280
LGATCVLKKKFSASQFWSQCKKYDVTVFQYIGELCRYLCK 320
OSKREGEKDHKVRLAIGNGIRSDVWREFLDRFGNIKVC 360
YAATESSISFMNYTGRIGAIGRTNLFYKLLSTFDLIK 400
410 420 430 440
QKDEPMRNEOGWCIVHKKGEPGLLISRVNAKNPFFGYAGP 440
YKHTKDKLLCDVFKKGDVYLNLTGDLIVQDDNLFYFWORT 480
GDTFRWKGENVATTEVADVIGMLDFIOEANYGVVAISGYE 520
GRAGMASIILKPNTSLDLKVEQVVTFLPAYACPRFLRI 560
QEKMEATGTFKLLKHOLVEDGFNPLKISEPLYFMONLKKS 600
610 620 630 640
YVLLTRELYDOI MLGEIKL. 620

Fig. 55

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mFATP1 full length.DNA

10 20 30 40
AAGTTCCCACTCCAGACTTCTGCGAGAACCCGTGAGGAAG 40
CAGCGAGAACCAGGGGTTTGCAAGCCAGAGAAGGATGCGG 80
ACTCCGGGAGCAGGAACAGCCTCTGTGGCTCATTGGGGC 120
TGCTTTGGCTTCTGGGACTTCCGTGGACCTGGAGCGCGGC 160
GGCGGCGTTCGGTGTGTACGTGGGTAGCGGTGGCTGGCGA 200
210 220 230 240
TTTCTGCGTATCGTCTGCAAGACGGCGAGGCGAGACCTCT 240
TTGGCTCTCTGTCTGATCCGCGTGGGCTAGAGCTACG 280
ACGACACCGGCGAGCAGGAGACACGATCCCACGCATCTTC 320
CAGGCCGTGCCCCAGCCACAGCCGGAGCGCCTGGCGCTGG 360
TAGATGCGAGTAGCGGTATCTGCTGGACCTTCGCACAGCT 400
410 420 430 440
AGACACCTACTCCAATGCTGTGGCCAATCTGTTCCCTCCAG 440
CTGGGCTTTGCGCCAGGCGATGTGGTGGCTGTGTTCCCTGG 480
AAGGCCGGCCCCGAGTTCGTGGGACTGTGGCTGGGCCCTGGC 520
CAAGGCCGGTGTAGTGGCTGCGCTTCTCAATGTCAACCTG 560
AGGCGGGAGCCCCCTGCGCTTCTGCTTGGGCACATCAGCTG 600
610 620 630 640
CCAAGGCCCTCATTATGGCGGGGAGATGGCAGCGGCGGT 640
GGCGGAGGTGAGTGAGCAGCTGGGGAAGAGCCTGCTCAAG 680
TTCTGCTCTGGAGATCTGGGGCCTGAGAGCGTCTTGCCTG 720
ACACGCAGCTTCTGGACCCCATGCTTGCTGAGGCGCCAC 760
CACACCCCTGGCACAGGCCCCAGGCAAGGGCATGGATGAT 800
810 820 830 840
CGGCTATTTTACATCTATACTTCTGGGACCACCGGACTTC 840
CTAAGGCGGCCATTGTGGTGCACAGCAGGTAACCGCAT 880
CGCAGCCTTCGGCCACCATTCTACAGCATGCGGGCCAAC 920
GATGTGCTCTATGACTGCCTACCTCTCTACCACTCAGCAG 960
GGAACATCATGGGCGTGGGACAGTGTATCATCTACGGGTT 1000
1010 1020 1030 1040
AACGGTGGTACTGCGCAAGAAGTTCTCCGCCAGCCGCTTC 1040
TGGGACGACTGTGTCAAATATAATTGCACGGTAGTGCAGT 1080
ACATCGGTGAAATATGCCGCTACCTGCTAAGGCAGCCGGT 1120
TCGCGATGTAGAGCGGCGGCACCGCGTGCCTGGCCGTG 1160
GGTAACGGACTGCGGCCAGCCATCTGGGAGGAGTTCACGC 1200

Fig. 56A

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mFATP1 full length.DNA

1210 1220 1230 1240
AGGGTTTCGGTGTCGACAGATTGGCGAGTTCTACGGCGC 1240
CACCGAATGCAACTGCAGCATTGCCAACATGGACGGCAAG 1280
GTCGGCTCCTGCGGCTTCAACAGCCGTATCCTCAGCATG 1320
TGTACCCCATCCGCTCTGGTCAAGGTCAACGAGGACACGAT 1360
GGAGCCACTGAGGGACTCCCAAGGCCTCTGCATCCCGTGC 1400

1410 1420 1430 1440
CAGCCCGGGGAACCTGGGCTTCTCGTGGGCCAGATCAACC 1440
AGCAAGACCCTCTGCGGCGCTTCGATGGCTATGTTAGTGA 1480
CAGCGCCACCAACAAGAAGATTGCCACAGCGTGTTCCGA 1520
AAGGGGACAGCGCCTACCTTTCAGGTGACGTGCTAGTGA 1560
TGGACGAGCTGGGGTACATGTACTTCCGTGACCGCAGCGG 1600

1610 1620 1630 1640
GGATACCTTCCGATGGCGCGGGCGAGAACGTATCCACCACG 1640
GAGGTGGAAGCCGTGCTGAGCCGCCGTGTGGGCCAGACGG 1680
ACGTGGCTGTGTATGGAGTGGCTGTGCCAGGAGTGGAGGG 1720
GAAAAGCGGCATGGCGGCCATTGCAGACCCCCACAACCAG 1760
CTGGACCCTAACTCAATGTACCAGGAATTGCAGAAGGTTT 1800

1810 1820 1830 1840
TTGCATCCTATGCCCAGCCCATCTTCCTGCGTCTTCTGCC 1840
CCAAGTGGATACAACAGGCACCTTCAAGATCCAGAAGACC 1880
CGACTACAGCGTGAAGGCTTTGACCCCCGCCAGACCTCAG 1920
ACCGGCTCTTCTTTCTAGACCTGAAACAGGGACGCTACCT 1960
ACCCCTGGATGAGAGAGTCCATGCCCCGCATCTGCGCAGGC 2000

2010 2020 2030 2040
GACTTCTCACTCTGAGCCTGGTGAGTGGGATGGCCCTGGA 2040
CTTGTGAGACCAGGGAGCCGGACACCCCTGTTTCAAGTGTT 2080
TCTCCTGCCTGGCCACGTGGCCAGCAGCACCTGTGGGTGC 2120
AGGAAACTGGAACCTGAGTGGCCGGGTGTCCCTTTCTTAC 2160
AACCACCATGCACACATCTAGCCTCTGCCTTGGTCTTTT 2200

2210 2220 2230 2240
TCTCCATCTCTTTCCTCCGTGCCCAGCAGGAGCCCCACAG 2240
ACACATTGGCTGCTGTGTCTTGCAGTGGGACCGGTGCTA 2280
GGGGTCCATGCTGCAGGCTGTGACCCGCACTGGTGCCAC 2320
CTCCCTTCCCCATTGTGCCTTAGGTTCTTCCACTGTGCGC 2360
CGGTGAAGCAAGTGGGGACCCACATAGCTGTTGTCCCTGC 2400

2410 2420 2430 2440
TGAGGGTTGGTAGCAAATGCACCCTCATGTGAGTGGGAG 2440
ACACATGCAGTCTCCCACTGACCCCCAATCAACTGAAGAT 2480
ACTGTTTGTATTATTGTTTTGAGATAGGGTCTCACTGTG 2520
GAGGCCAAGCTGGCCTCAGGCTCACCCTCTACTGCCTCC 2560
GGGCACCAGCCTGCAGTTTGATGACATGTATGCACATTG 2600

Fig. 56B

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mFATP1 full length.DNA

```
      2610      2620      2630      2640
TTCTAAGGGTCTTCTGAGTCCCTGCTTTCCCCTCATGTCC 2640
TAAACCTTCCAGAACTGACTCTGATCACTTGGATGTAGC 2680
TAGTGTGGCCCTGCCCACGTGTGTCAATTCAGGGGTCCC 2720
CAGGCATCATCTCTGGAGGCCCTAACCTTGGCAAAGCTTG 2760
GATGTCCTCACATCAACAGCAGGAGACCCAGGAAGGTTGCT 2800
      2810      2820      2830      2840
GTGGTGTCTCTTGGGCACCCCTGGCGGCAGCCGTGGACAT 2840
GCTTCCCTGCTGTGATAGCCCAAACCTGTTGCCTATGACAT 2880
TTGAGGTCTACCCTTCTGGCTGCCATGGTCCCCATTGAGA 2920
TCTTTGGTGACTCACCTCAGCCACCAAGCCAGGCCTCTGC 2960
CTTCCTTCAGCTCTAAGGGCATGAAGGGTGTGGACAGAGC 3000
      3010      3020      3030      3040
AGCCACAGGCTGCCCACAGTCACCCACATGCAAGTGTTAT 3040
TTCCTTGTTTGTGTTTTAAAAAATAAACATGCTGAGCCTTG 3080
AAAAAAAAAAAAAAAAAAAA 3096
```

Fig. 56C

mFATP1 full lenght.protein

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10 20 30 40
MRTPGAGTASVASLGLLWLLGLPWTWSAAAAGVYVCGSGG 40
WRFLRIVCKTARRDLFGLSVLIRVRLELRRHRRAGDTIPR 80
IFOAVAOROPERLALVDASSGICWTFAOLDTYSNAVANLF 120
LOLGFAPGDVVAVFLEGRPEFVGLWLGLAKAGVVAALLNV 160
NLRREPLAFCLGTSAAKALIYGGEMAAVAEVSEOLGKSL 200
210 220 230 240
LKFCSGDLGPESVLPDTOLLDPMLAEAPTTPLAQAPGKGM 240
DDRLFYIYTS GTTGLPKAAIVVHSRYRIA AFGHHSYSMR 280
ANDVLYDCLPLYHSAGNIMGVGOCLIIYGLTVVL RKKFSAS 320
RFWDDCVKYNCTVVOYIGEICRYLLROPVRDVERRHRVRL 360
AVGNGLRPAIWEEFTOGFGVROIGEFYGATECNCSIANMD 400
410 420 430 440
GKVGSCGFNSRILTHVYPJRLVKVNEOTMEPLRDSOGLCI 440
PCOPGEPGLLVGOINQODPLRRFDGYVSDSATNKKIAHSV 480
FRKGDSAYLSGDVLMDELGYMYFRDRSGDTFRWRGENVS 520
TTEVEAVLSRLLGOTDVAVYGVAVPGVEGKSGMAAIADPH 560
NOLDPNMSMYOELOKVLASYAOPIFLRLLPOVDTTGTFKIQ 600
610 620 630 640
KTRLOREGFDPROTS DRLFFLDLKOGRYLPDERVHARIC 640
AGDFSL. 647

Fig. 57

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mVLACS(FATP2)full length.DNA

10 20 30 40
GACACAGTACTGCCGATGTTGGACAGAGGATCGCTTAACA 40
GAACGAAATCTCAAAACAAATTAACAGGACCCGGTTGCTT 80
GATTTCCCAAATCAGAAAAGGCTCGAAATGTCTAGAGGGG 120
CTGACTGATGCAGCGGTGACCCGGACTGGAGACAGTTGGA 160
CGCGATCATCTCTGGTGCTTTTGTTC AACCTTGAAACCTT 200
210 220 230 240
CGCCACAGGAGACTTGCTGAGCAGAGAAGCAAACGTGGA 240
GAAACAAAGAGAGATCTAGCGAAAAGCCTCTGGGACCAAG 280
GAGGGGAGGTGGGACTCTGGGTTGGCGGTGGCACCTGCTG 320
CCGGCTATTAATAATAGGGTCGCGATGCGTTTATAAGGTG 360
TTTGATTAAACAAAGACTCTATGAGAGAAGAATAACTAGC 400
410 420 430 440
AACAGCCCCACGTCTGAGTCGTGCGCTCCGACCTTTTTTCA 440
ACGTGGGTTCTTTGGGCCGAGCGTCGTTTGCCGAGAACTA 480
GATCTCACCTGACCCCAAGCTGACAAAGGCGCGCCCCCTGA 520
CATCCTGGGCCACCCCAAGCTGACAAAGGCGCGCCCCCTGA 560
GCACACGAGGTGCCCCACGAGGGGAGGGACCCACAGCCG 600
610 620 630 640
TCCCGCCCGCACC GCGGTGTCCGCTGCGGGCACCTGCAGC 640
CGAGCCGCCACCCG CAGTCGCGAGCGGTCCGGCGGCCGAA 680
CCCGGTGCTCAGCTCGTCAGCACCTGCTCTGCTTCTCTCC 720
CGCCCGCCGCCGCGCTGCACGCCCTCGAGCGCTCCCTCGGC 760
CCCGGCGGGGACC GGGGACCCCGCAGCCACCGCCATGCTG 800
810 820 830 840
CCTGTGCTCTACACCGGCTGGCGGGGCTGCTGCTGCTGC 840
CTCTGCTGCTCACCTGCTGCTGCCCCCTACCTCCTCCAGGA 880
CGTGCGGTTCTTCCCTGCAACTGGCCAAACATGGCCCGGCAG 920
GTGCGCAGCTACCGGCAGCGGCGACCCGTGCGCACCATCC 960
TGCATGTCTTCTTGGAGCAAGCGCGCAAGACCCCGCACAA 1000
1010 1020 1030 1040
GCCCTTCCTGCTGTTTCGCGACGAGACGCTTACCTACGCC 1040
CAGGTAGACCGGCGCAGCAACCAAGTAGCGCGAGCGCTGC 1080
ATGATCACCTGGGCTGCGGCAGGGGGATTGCGTGGCCCT 1120
CTTCATGGGCAATGAGCCGGCCTACGTGTGGCTCTGGCTG 1160
GGACTGCTCAAACTGGGCTGTCCCATGGCGTGCCTCAACT 1200

Fig. 58A

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mVLACS(FATP2)full length.DNA

```

      1210      1220      1230      1240
      | | | | | | | | | | | | | | | |
ACAACATCCGTGCCAAGTCTCTGCTACACTGCTTTTCAGTG 1240
CTGCGGGGCGAAGGTGCTGCTGGCCTCCCCAGAGCTACAC 1280
GAAGCTGTGCGAGGAGGTTCTTCCAACCTGAAAAAGGAGG 1320
GCGTGTCCGTCTTCTACGTAAGCAGAACTTCTAACACTAA 1360
TGCGCTGGACACAGTACTGGACAAAGTAGACGGGTGTCTG 1400
      1410      1420      1430      1440
      | | | | | | | | | | | | | | | |
GCGGACCCCATCCCGGAGTCGTGGAGGTCTGAAGTCACGT 1440
TCACCACACCCGCAGTCTACATATATACTTCGGGCACCAC 1480
AGGTCTTCCAAAGGCTGCAACCAATTAATCACCATCGCCTC 1520
TGGTATGGGACCAGCCTTGCCCTGAGGTCCGGAATTAAGG 1560
CTCATGACGTCATCTACACCACCATGCCCCGTGTACCACAG 1600
      1610      1620      1630      1640
      | | | | | | | | | | | | | | | |
CGCGGCGCTCATGATTGGCCTCCACGGATGCATTGTGGTT 1640
GGGGCTACATTTGCTTTGCGGAGCAAATTTTCAGCCAGCC 1680
AGTTTTGGGACGACTGCAGGAAATACAACGCCACTGTCTAT 1720
TCAGTACATCGGTGAACTGCTTCGGTACCTCTGCAACACG 1760
CCCCAGAAACCAAATGACCGGGACCACAAAGTAAAAATAG 1800
      1810      1820      1830      1840
      | | | | | | | | | | | | | | | |
CACTAGGAAATGGCTTACGAGGAGATGTGTGGAGAGAGTT 1840
CATCAAGAGATTTGGGGACATTCACATTTATGAGTTCTAC 1880
GCTTCCACTGAAGGCAACATTTGGATTTATGAACTATCCAA 1920
GAAAAATCGGAGCTGTTGGAAGAGAAAAATTACCTACAAAA 1960
AAAAGTTGTAAGGCACGAGCTGATCAAGTATGACGTGGAG 2000
      2010      2020      2030      2040
      | | | | | | | | | | | | | | | |
AAGGATGAGCCTGTCCGTGATGCAAATGGATATTGCATCA 2040
AAGTCCCCAAAGGAGAGGTTGGACTCTTGATTTGCAAAAT 2080
CACAGAGCTCACACCATTTTTTGGCTATGCTGGAGGAAAG 2120
ACCCAGACAGAGAAGAAAAAGCTCAGAGATGTTTTTAAGA 2160
AAGGAGACGTCTACTTCAACAGTGGCGATCTCCTGATGAT 2200
      2210      2220      2230      2240
      | | | | | | | | | | | | | | | |
CGACCGTGAAAAATTTTCATCTATTTTCACGACAGAGTTGGA 2240
GACACCTTCCGGTGGAAGGAGAGAAATGTASCTACCACGG 2280
AAGTCGCTGACATTGTGGGACTGGTAGATTTTGTGAAGA 2320
AGTGAATGTTTACGGTGTGCCCCGTGCCAGGTCATGAAGGT 2360
CGCATCGGGATGGCCTCGATCAAGATGAAAGAAAACCTACG 2400
      2410      2420      2430      2440
      | | | | | | | | | | | | | | | |
AGTTCAATGGAAGAAACTCTTTTACGACATCTCGGAGTA 2440
CCTGCCAGTTACTCGAGGCCTCGGTTCTTGAGAATACAA 2480
GATACCATTGAGATCACCGGGACTTTTAAACACCGCAAAG 2520
TGACCTGATGGAAGAGGGCTTTAACCCCTCAGTCATCAA 2560
AGATACCTTGTATTTTCATGGATGACACAGAAAAAACATAC 2600

```

Fig. 58B

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mVLACS(FATP2)full length.DNA

2610 2620 2630 2640

GTGCCCATGACTGAGGACATTTATAATGCCATAATTGATA 2640
AGACTCTGAAGCTCTGAATGTTGCCTGGCTCCTAACACTT 2680
CCAGAAAGAAACACAATAGGCCTAGCATAGCCCCCTTCACA 2720
TGTGTAATCCAACCTTTAACTTGATTAAAGGTTATAGGTGT 2760
GATTTTTCCTAGGAAATTATTCATTTAAAGGACAATTGTT 2800

2810 2820 2830 2840

TGTTTGTTTGTTTGTTTTTATTAAATTACACCAGAACGTT 2840
TGCAAGTAAAAAGATTTAAAGTCACTTATTTTTCAATGTG 2880
CACCTGCCATTTGTCCTTGCAAACCTTAGCTTCTTGGAGAG 2920
AGGGCCTTATTTTTTTAAAGACATAATAAACTATGTAAAC 2960
ACT 2963

Fig. 58C

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mVLACS(FATP2)full length.prot

```
      10      20      30      40
MLPVL YTGLAGLLLLPLLLTCCCPYLLQDVRF FLOLANMA 40
ROVRSYRORRPVRTILHVFLEOARKTPHKPFLLFRDET LT 80
YAQVDRRSNOVARALHDHLGLROGOCVALFMGNEPAYVWL 120
WLG L LKLGCPMACLNYNIRAKSLLHCFQCCGAKVLLASPE 160
LHEAVEEVLP TLKKEGVSVFYVSRTSNTNGVDTVLDKVDG 200
      210      220      230      240
VSADPIPESWRSEVFTTPAVYIYTS GTTGLPKAATINHH 240
RLWYGTSLALRSGIKAHQVIYTTMP LYHSAALMIGLHGC I 280
VVGATFALRSKFSASQFWDDCRKY NATVIOYIGELLRYLC 320
NTPOKPNDRDHKVKIALGNGLRGDVWREFIKRFGDIHIYE 360
FYASTE GNIGFMNYPRKIGAVGRENYLOKKVVRHEL I KYD 400
      410      420      430      440
VEKDEPVRDANGYCIKVPKGEVGLL ICKITELTPFFGYAG 440
GKTOTEKKKL RDVFKKGDVYFN SGDLLMIDRENFIYFHDR 480
VGDTFRWKGENVATTEVADIVGLVDFVEEVN VYGVPVPGH 520
EGRIGMASIKMKENYEFNGKKLFQHI SEYLPYSRPRFLR 560
IODTIEITGTFKHKRVTLMEEGFNPSVIKDTLYFMDDTEK 600
      610      620      630      640
TYVPMTEDIYNAIIDKTLKL. 621
```

Fig. 59

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rnFATP4 partial.DNA

10 20 30 40
GATCAGCTCTTCTATATCTACACGTCGGGACCCACGGGGC 40
TACCCAAAGCTGCCATTGTGGTGACAGCAGGTATTACCG 80
AATGGCTGCCCTGGTGTACTATGGATTCCGCATGCGGCCT 120
GATGACATTGTCTATGACTGCCTCCCCCTCTACCACTCAG 160
CAGGAAACATTGTGGGGATTGGCCAGTGCGTACTCCACGG 200
210 220 230 240
CATGACTGTGGTGATCCGGAAGAAGTTTTAGCCTCCCGG 240
TTCTGGGATGACTGTATCAAGTACAACGACAAATTGTAC 280
AGTACATTGGTGAGCTTTGCCGCTACCTCCTGAACCAGCC 320
ACCCCGTGAGGCTGAGTCTCGGCACAAGGTGCGCATGGCA 360
CTGGGCAACGGTCTCCGGCAGTCCATCTGGACCGACTTCT 400
410 420 430 440
CCAGCCGTTTTCCACATTCCCAAGGTGGCCGAGTTCTACGG 440
GGCCACCGAGTGCAACTGTAGCTTGGGCAACTTTGACAGC 480
CAGGTGGGGGCTGTGGCTTCAATAGCCGCATCCTGTCCT 520
TTGTGTACCCCATCCGCTTGGTACGAGTCAATGAGGATAC 560
CATGGAACCTGATCCGGGGACCCGATGGCGTCTGCATTCCC 600
610 620 630 640
TGTCACACAGGCCAGCCAGGCCAGCTGGTGGGTGCGATCA 640
TCCAGCAGGACCCCTACGCCGTTTTGATGGCTACCTCAA 680
CCAGGGTGCCAACAACAAGAAGATTGCTAGTGATGTCTTC 720
AAGAAAGGGGACCAAGCCTACCTCACTGGTGACGTGCTGG 760
TGATGGATGAGCTGGGCTACCTGTACTTCCGAGACCGCAC 800
810 820 830 840
AGGGGACACGTTCCGCTGGAAAGGGGAGAATGTGTCTACC 840
ACTGAAGTGGAGGGCACACTCAGCCGCTGCTTCAGATGG 880
CAGATGTGGCTGTTTATGGTGTGAGGTGCCAGGAGCTGA 920
GGGCCGAGCAGGAATGGCTGCTGTGGCAAGCCCCACTAGC 960
AACTGTGACCTGGAGAGCTTTGCACAGACCTTGAAAAAGG 1000
1010 1020 1030 1040
AGCTGCCCCGTGACGCCCGCCCCATCTTCTCCGCTTCTT 1040
GCCTGAGCTGCACAAAACAGGAACCTTCAAGTTCAGAAG 1080
ACAGAGTTGCGGAAGGAGGGCTTTGACCCGCTGTGTGTA 1120
AAGACCCACTCTTCTATTTGGATGCCCCGACAGGCTGCTA 1160
TGTTGCACTGGACCAAGAGGCCTATACCCGCATCCAGGCA 1200

Fig. 60A

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mFATP4 partial.DNA

1210 1220 1230 1240

GGCGAGGAGAAGCTGTGATTTCCCCCACATCCCTCTGAGG 1240
GCCAGAGGATGCTGGATTCAGAGCCCCAGCTTCCACTCCA 1280
GAAGGGGTCTGGGCAAGGCCAGACCAAAGCTAGCAGGGGCC 1320
CGCACCTTCACCCTAGGTGCTGATCCCCCT 1350

Fig. 60B

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mFATP4partial.DNA

10 20 30 40
DOLFYIYTS GTTGLPKAAIVVHSRYRMAALVYYGFRMRP 40
DDIVYDCLPLYHSAGNIVGIGOCVLHGMTVVIRKKFSASR 80
FWDDCIKYNCTIV OYIGELCRYLLNOPPREAESRHKVRMA 120
LGNGLRQSIWTD FSSRFHIPKVAEFYGATECNC SLGNFDS 160
QVGACGFNSRILSFVYPIRLVRVNEDTMELIRGPDGVCIP 200
210 220 230 240
COPGQPGQLVGR IIOQDPLRRFDGYLNOGANNKKIASDVF 240
KKGDOAYLTGDVLVMD ELGYLYFRDRTGDTFRWKGENVST 280
TEVEGTL SRLLOMADVAVYGVEVPGAEGRAGMAAVASPTS 320
NCDLESFAOTLKKELPLYARPIFLRFLPELHKTGTFKFQK 360
TELRKEGFDP SVVKDPLFYLDARTGCYVALDOEAYTRIOA 400
410 420 430 440
GEEKL. 406

Fig. 61

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mmFATP1 full length.DNA

```

      10      20      30      40
      |      |      |      |
ATGCGGGCTCCTGGAGCAGGAACAGCCTCTGTGGCCTCAC 40
TGGCGCTGCTTTGGTTTCTGGGACTTCCGTGGACCTGGAG 80
CGCGGCGGGCGGCGTTCGTGTGTACGTGGGTGGCGGCGGC 120
TGGCGCTTTCTGCGTATCGTCTGCAAGACGGCGAGGCGAG 160
ACCTCTTTGGCCTCTCTGTTCTGATTTCGTGTTGGGCTAGA 200
      210      220      230      240
      |      |      |      |
GCTGCGACGACACCGGCGAGCAGGAGACACGATCCCGTGC 240
ATCTTCCAGGCTGTGGCCCGGCGACAACCAGAGCGCCTGG 280
CACTGGTGGACGCCAGTAGTGGTATATGCTGGACCTTCGC 320
ACAGCTGGACACCTACTCCAATGCTGTAGCCAACCTGTTC 360
CGCCAGCTGGGCTTTGCACCAGGCGATGTGGTGGCTGTGT 400
      410      420      430      440
      |      |      |      |
TCCTGGAGGGCCGGCCGGAGTTCTGTGGGACTGTGGCTGGG 440
CCTGGCCAAGGCCGGTGTGGTGGCTGCTCTTCTCAATGTC 480
AACCTGAGGCGGGAGCCCCCTGGCCTTCTGCCTGGGCACAT 520
CAGCTGCCAAGGCCCTCATTTATGGCGGGGAGATGGCAGC 560
GGCGGTGGCGGAGGTGAGCGAGCAGCTGGGGAAGAGCCTC 600
      610      620      630      640
      |      |      |      |
CTCAAGTTCTGCTCTGGAGATCTGGGGCCTGAGAGCATCC 640
TGCTTGACACGCAGCTCCTGGACCCCATGCTTGCTGAGGC 680
GCCCCACACACCCCTGGCACAAGCCCCAGGCAAGGGCATG 720
GATGATCGGCTGTTTTACATCTATACTTCTGGGACCACCG 760
GGCTTCCTAAGGCTGCCATTGTGGTGCACAGCAGGTAATA 800
      810      820      830      840
      |      |      |      |
CCGCATTGCTGCCCTTTGGCCACCATTCCTACAGCATGCGT 840
GCCGCCGATGTGCTCTATGACTGCCTGCCACTCTACCACT 880
CTGCAGGGAACATCATGGGTGTGGGGCAGTGCATCATCTA 920
CGGGTTGACGGTGGTACTGCGCAAGAAGTTCTCCGCCAGC 960
CGCTTCTGGGATGACTGTGTCAAGTACAATTGCACGGTAG 1000
      1010      1020      1030      1040
      |      |      |      |
TGGATGACATAGGTGAAATCTGCCGCTACCTGCTGAGGCA 1040
GCCGGTTGCGGACGTGGAGCAGCGACACCGGTGCGCCTG 1080
GCCGTGGGTAATGGGCTGCGGCCAGCCATCTGGGAGGAGT 1120
TCACGCAGCGCTTCGGTGTGCCACAGATCGGCGAGTTCTA 1160
CGGCGCTACCGAGTGCAACTGCAGCATTGCCAACATGGAC 1200

```

Fig. 62A

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mmFATP1 full length.DNA

```

      1210      1220      1230      1240
      | | | | | | | | | | | | | | | |
GGCAAGGTCGGCTCCTGCGGCTTCAACAGCCGTATCCTCA 1240
CGCATGTGTACCCCATCCGTCTGGTCAAGGTCAATGAGGA 1280
CACGATGGAGCCACTGCGGGACTCCGAGGGCCTCTGCATC 1320
CCGTGCCAGCCCGGGGAACCCGGCCTTCTCGTGGGCCAGA 1360
TCAACCAGCAGGACCCTCTGCGGCGTTTCGATGGTTATGT 1400

      1410      1420      1430      1440
      | | | | | | | | | | | | | | | |
TAGTGACAGTGCCACCAACAAGAAGATTGCCCACAGCGTT 1440
TTCCGAAAGGGCGATAGCGCCTACCTCTCAGGTGACGTGC 1480
TAGTGATGGACGAGCTGGGCTACATGTATTTCCGTGACCG 1520
CAGCGGGGACACCTTCCGCTGGCGCGGGGAGAACGTGTCC 1560
ACCACGGAGGTGGAAGCCGTGCTGAGCCGCCTACTGGGCC 1600

      1610      1620      1630      1640
      | | | | | | | | | | | | | | | |
AGACGGACGTGGCTGTGTATGGGGTGGCTGTGCCAGGAGT 1640
GGAGGGGAAAGCTGGCATGGCAGCCATCGCAGATCCCCAC 1680
AGCCAGTTGGACCCTAACTCAATGTACCAGGAATTACAGA 1720
AGGTTCTTGCATCCTATGCTCGGCCCATCTTCTTGCCTCT 1760
TCTGCCCCAGGTGGATACACAGGCACCTTCAAGATCCAG 1800

      1810      1820      1830      1840
      | | | | | | | | | | | | | | | |
AAGACCCGGCTGCAGCGTGAAGGCTTTGACCCCGTCAGA 1840
CCTCAGACAGGCTCTTCTTTCTAGACCTGAAGTCCGGCAC 1880
GAGGTATCTACCCCTGGATGAGAGAGTCCATGCCCGCATT 1920
TGCGCAGCGCACTTCTCACTCTGAGCCTGGAGAGTGGGCT 1960
GGGCCTGGACTCCTGAGACCTGGGAGCCTGACACCCCTCT 2000

      2010      2020      2030      2040
      | | | | | | | | | | | | | | | |
TCGGGTGCTTCTCCTGCCTGGCCACATGGACAGCAGCACC 2040
TGTGAGAGTAGGAAAATGGAACCTGAGTGGCTGGGACCCC 2080
TCTCCTACTTCCCACTATGCATCCATTTTGCCCTCTGCCTT 2120
GATCTTTTTTCTCCATCTCTTTTCTCCCTACCCAGCAGGAG 2160
CCCCACAAACACATGTTGGCTGCTGTGTCCTGCAGTTGGA 2200

      2210      2220      2230      2240
      | | | | | | | | | | | | | | | |
CCAGTGTCAGGGGTACAGGCTTCAGGCTGTGACCCACAC 2240
TGGTACCCACCTCCCTTTCTTATTTTGCTTAGGTTTCATC 2280
CACGGTTCCCTGTGGAGCAAGTGGGGGCCACATAGCTG 2320
CTGTCCCTGCTGAGGGTTGGTAGCAATCACACCCCTCATGT 2360
CAGCTGGGAGACACGCGCAGTCTCCCACTGACCCCCAATC 2400

      2410      2420      2430      2440
      | | | | | | | | | | | | | | | |
AACTGAAAATATTGTTTTGACTACTTTTTGTTTTTTTGTT 2440
TTTTTGTTTTTTTTTTTTTTTCGAGACAGAGTTTCTCTGTA 2480
TAGCCCTGGCTGTCTTGGAACTCACTTTGTAGACCAGGCT 2520
GGCCTCGAACTCAAAAATCCTCTGACTCTGCCTCTGCTT 2560
CCCAAGTGCTGGGATTAAAGACGTGCGCCACCACCGCCTG 2600

```

Fig. 62B

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mmFATP1 full length.DNA

2610	2620	2630	2640
GCTGTTTTGTATTTTGTGTTTGTGTTTGTGACGATAGGGTCTC 2640			
ACTGTGGAGGCCAAGCTGGCCTCAGACTCCCCACCCATT 2680			
GCCTCTGGGCACCATTTCTATATTCTCAGACTGATGACAAT 2720			
GCACTAGTGTCCCTAGGAGTCTTGAGTCTGCACTTTCCTC 2760			
TCATAGCCTCAAGCTTCCAGAACTGACTCTGATCACTTGG 2800			
2810	2820	2830	2840
ATGTGGCTAGTGTGGCTCTACCCACATGTGTCAATTCAG 2840			
GGGTCCCCAGGCATAGTCTCTGGAAGCCCTCACCCGAAAA 2880			
AAGCTTGGAGAGACCCAGGAAGGTTGTTGTGTTCTCTTGG 2920			
GCACCCCTGGTGGCAGTCCTGGGCATGCTTCCGCACTGT 2960			
ACTGGTGCATATAGCCCAGACCTATGACATTTGAGGTCTA 3000			
3010	3020	3030	3040
CCCTTCTGGCTCCTGTGGTCCCCATTGAGATCCTTGGTGA 3040			
CTCACCTCAGTCACCAAGCAGAGCCTCTGCCTGCCTTCAT 3080			
CTTCAAGGTCATGAAGGATGTGGACAGAGCAGCTACAGGC 3120			
TGCCAGCAGTCAACCACATGAGAGTGTTACTTCTTGTG 3160			
GTTTTTAAAAAATAAATGTGCTGAGCCTCGAAAAAAAAAA 3200			
3210	3220	3230	3240
AAAAAAAAAAAAAAAAA 3217			

Fig. 62C

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mmFATP1 full length.protein

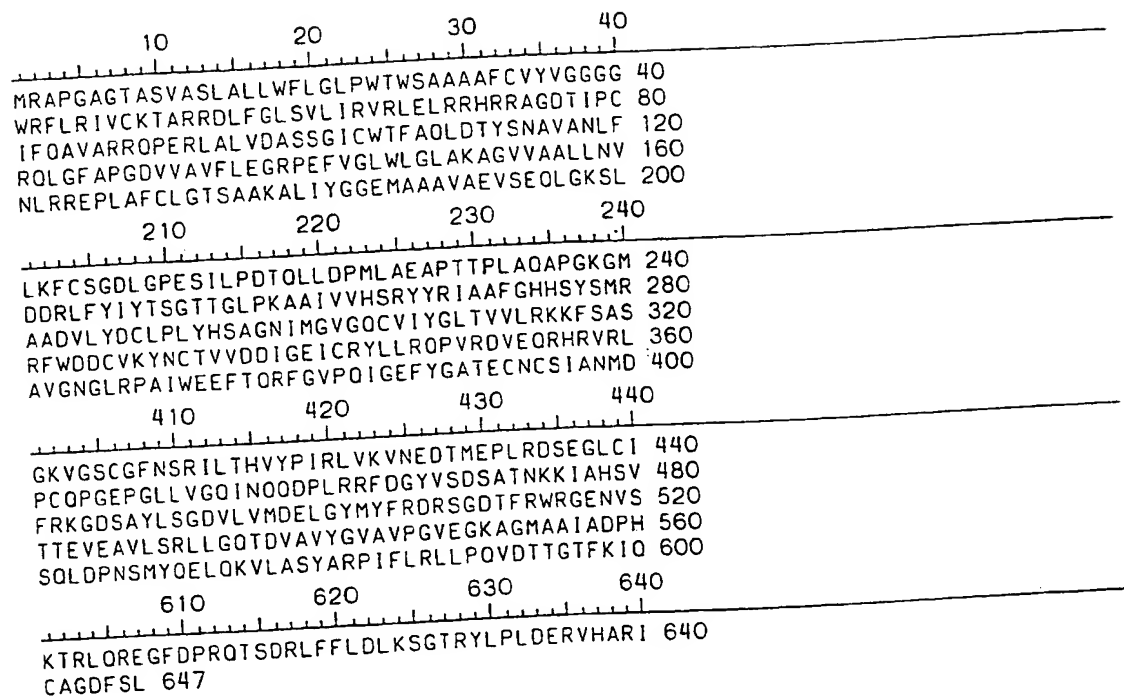


Fig. 63

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mmFATP2 full length.DNA

```

      10      20      30      40
      |      |      |      |
GGGCGGAGGCCGAGCCAGTCGCCAGCTCCTGCTCTGCTC 40
CTCTCCCGCCTGCCGCGCGCTGCACGCCCTCGAGCACTCC 80
CTCGGCCCCGGCGGGGACCGGGGACCCCGCAGCTACCGCC 120
ATGCTGCCAGTGCTCTACACCGCCTGGCGGGGCTGCTGC 160
TGCTGCCCTCTGCTGCTCACCTGCTGCTGCCCCCTACCTCCT 200

      210      220      230      240
      |      |      |      |
CCAAGATGTGCGGTACTTCTTGCGGCTGGCCAACATGGCC 240
CGGCGGGTGCGCAGCTACCGGCAGCGGCGACCCGTGCGTA 280
CCATCCTGCGGGCCTTCTTGGAACAAGCGCGCAAGACCCC 320
ACACAAGCCCTTCTTGCTGTTCCGAGACGAGACGCTCACC 360
TACGCCCAGGTGGACCGGCGCAGCAACCAAGTGGCGCGGG 400

      410      420      430      440
      |      |      |      |
CGCTGCACGATCAACTGGGCCTACGACAGGGGGATTGCGT 440
AGCCCTCTTTCATGGGCAATGAGCCGGCCTACGTGTGGATC 480
TGGCTGGGACTGCTCAAACCTGGGCTGTCCCATGGCGTGCC 520
TCAACTACAACATTCGTGCCAAGTCTCTGCTGCACTGCTT 560
TCAATGCTGCGGGGCGAAGGTGCTGCTGGCCTCCCCAGAT 600

      610      620      630      640
      |      |      |      |
CTACAAGAAGCTGTGGAGGAGGTTCTTCCAACCCTGAAAA 640
AGGATGCCGTGTCCGTCTTTTACGTAAGCAGAACTTCTAA 680
CACAAATGGTGTGGACACAATACTGGACAAAGTAGACGGA 720
GTGTCGGCGGAACCCACCCCGGAGTCGTGGAGGTCTGAAG 760
TCACTTTACCACGCCAGCAGTATACATTTATACTTCGGG 800

      810      820      830      840
      |      |      |      |
AACCACAGGTCTTCCAAAAAGCGGAACCATCAATCATCAT 840
CGCCTAAGGTATGGGACAAGCCTTGCTATGTGCGAGTGGGA 880
ATCACGGCCAAGGATGTCATCTATACCAACAATGCCCCCTG 920
TTCCAACAGTGCAACGCTCAAGATCGGCCTTACGGATGC 960
ATCCTGGGTTGGGGCTACTTTAACCTTGGCGGGGCAAATT 1000

      1010      1020      1030      1040
      |      |      |      |
CTCAAGCAAGCCAATTTTGGGAACGACTGGCAGGAAATAC 1040
AACGTCAACGGTCATTCAGTACATTGGTGAACCTGCTTCGG 1080
TACCTGTGCAACACACCGCAGAAACCAAAATGACCGGGACC 1120
ACAAAAGTGAAAAAAGCCCTGGGAAATGGCTTACGAGGAGA 1160
TGTTGTGAGAGAGTTTCATCAAGAGATTTGGGGACATCCAC 1200

```

Fig. 64A

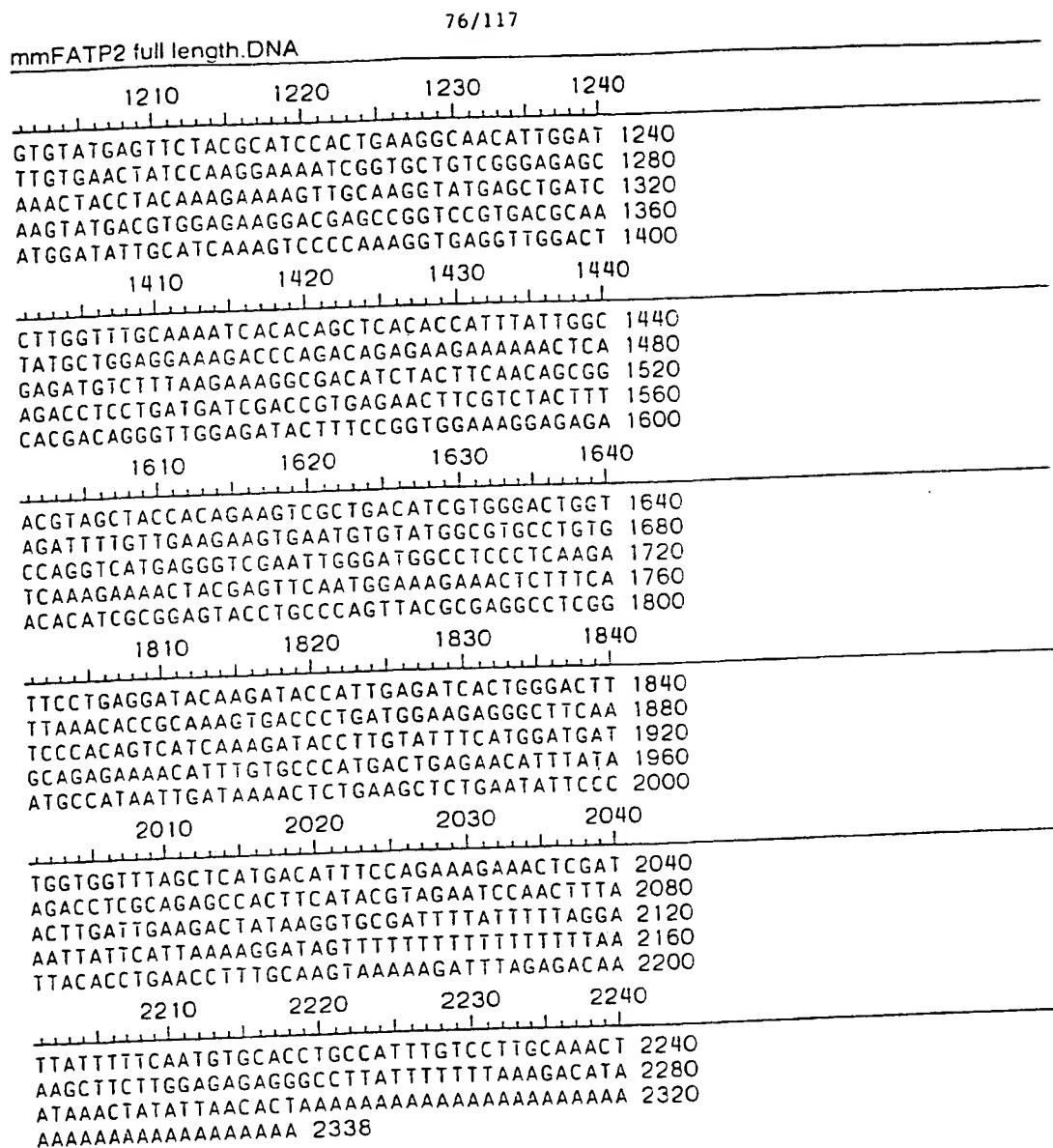


Fig. 64B

mmFATP2 full length.protein

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10 20 30 40
MLPVLYTGLAGLLLLPLLLTCCCPYLLQDVRYFLRLANMA 40
RRVRSYRORRPVRTILRAFLEQARKTPHKPFLFRDETTLT 80
YAOVDRRSNOVARALHDOLGLROGDCVALFMGNEPAYVWI 120
WLGLLKLGCMACLNYNIRAKSLLHCFQCCGAKVLLASPD 160
LOEAVEEVLPTLKKDAVSFVYSRTSNTNGVDITLDKVDG 200
210 220 230 240
VSAEPTPESWRSEVTFTTPAVYIYTSGTTGLPKSGTINHH 240
RLRYGTSLAMSSGNHGOGCHLYOOCPCSNSATLKI GLHGC 280
ILGWGYFNLGGANSOASQFVERLAGNTTSTVIOYIGELLR 320
YLCNTPOKPNDRDHKVKKALGNGLRGDVWREFIKRFGDIH 360
VYEFYASTEIGNIGFVNYPRKIGAVGRANYLORKVARYELI 400
410 420 430 440
KYDVEKDEPVRDANGYCIKVPKGEVGLLVCKITOLTPFIG 440
YAGGKTQTEKKKLROVFKKGDYFNSGDLLMIDRENFVYF 480
HDRVGDTRFWKGENVATTEVADIVGLVDFVEEVNYYGVPV 520
PGHEGRIGMASLKIKENYEFNGKKLFQHIAEYLPSYARPR 560
FLRIODTIEITGTFKHKRVTLMEEGFNPTVIKDTLYFMDD 600
610 620 630 640
AEKTFVPMTENIYNATIDKTLKL 624

Fig. 65

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mmFATP3 partial.DNA

10 20 30 40
GAAAGCTCTGAGAGCGGGTGCAGTCTGGCCTGGCGTCTCG 40
CGTACCTGCCCCGGGAGCAGCCGACACACACCTTCCTCAT 80
CCACGGCGCGCAGCGCTTTAGCTACGCGGAGGCTGAGCGC 120
GAGAGCAACCGGATTGCTCGCGCCTTTCTGCGCGCACGG 160
GCTGGACCGGGGGCCGCCGAGGCTCGGGCAGGGGCAGCAC 200
210 220 230 240
TGAGGAAGGCGCACGCGTGGCGCCTCCGGCTGGAGATGCG 240
GCTGCTAGAGGGACGACCGCGCCCCCTCTGGCACCCGGGG 280
CGACCGTGGCGCTGCTCCTCCAGCGGGCCCGGATTTCCT 320
TTGGATTTGGTTCCGACTGGCCAAAGCTGGCCTGCGCACG 360
GCCTTTGTGCCACCGCTTTACGCCGAGGACCCCTGCTGC 400
410 420 430 440
ACTGCCTCCGCAGCTGCGGTGCGAGTGCCTCGTGCTGGC 440
CACAGAGTTCTTGGAGTCCCTGGAGCCGGACCTGCCGGCC 480
TTGAGAGCCATGGGGCTCCACCTATGGGCGACGGGCCCTG 520
AAACTAATGTAGCTGGAATCAGCAATTTGCTATCGGAAGC 560
AGCAGACCAAGTGGATGAGCCAGTGCCGGGGTACCTCTCT 600
610 620 630 640
GCCCCCAGAACATAATGGACACCTGCCTGTACATCTTCA 640
CCTCTGGCACTACTGGCCTGCCCAAGGCTGCTCGAATCAG 680
TCATCTGAAGGTTCTACAGTGCCAGGGATTCTACCATCTG 720
TGTGGAGTCCACCAGGAGGACGTGATCTACCTCGCACTCC 760
CACTGTACCACATGTCTGGCTCCCTTCTGGGCATTGTGGG 800
810 820 830 840
CTGCTTGGGCATTGGGGCCACCGTGGTGCTGAAACCCAAG 840
TTCTCAGCTAGCCAGTTCTGGGACGATTGCCAGAAACACA 880
GGGTGACAGTGTTCAGTACATTGGGGAGTTGTGCCGATA 920
CCTCGTCAACCAGCCCCGAGCAAGGCAGAGTTTGACCAT 960
AAGGTGCGCTTGGCAGTGGGCAGTGGGTTGCGCCAGACA 1000
1010 1020 1030 1040
CCTGGGAGCGTTTCTGCGGCGATTTGGACCTCTGCAGAT 1040
ACTGGAGACGTATGGCATGACAGAGGGCAACGTAGCTACG 1080
TTCAATTACACAGGACGGCAGGGTGCAGTGGGGCGAGCTT 1120
CCTGGCTTTACAAGCACATCTTCCCTTCTCCTTGATTCTG 1160
ATACGATGTCATGACAGGGGAGCCTATTCTGGAATGCCCAG 1200

Fig. 66A

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mmFATP3 partial.DNA

1210	1220	1230	1240
GGGCACTGCATGACCACATCTCCAGGTGAGCCAGGCCTAC 1240			
TGGTGGCCCCAGTGAGCCAGCAGTCCCCCTTCCTGGGCTA 1280			
TGCTGGGGCTCCGGAGCTGGCCAAGGACAAGCTGCTGAAG 1320			
GATGTCTTCTGGTCTGGGGACGTTTTCTTCAATACTGGGG 1360			
ACCTCTTGGTCTGTGATGAGCAAGGCTTTCTTCACTTCCA 1400			
1410	1420	1430	1440
CGATCGTACTGGAGACACCATCAGGTGGAAGGGAGAGAAT 1440			
GTGGCCACAACCTGAAGTGGCTGAGGTCTTGGAGACCTTGG 1480			
ACTTCCCTTCAGGAGGTGAACATCTATGGAGTCACGGTGCC 1520			
AGGGCACGAAGGCAGGGCAGGCATGGCGGCCTTGGCTCTG 1560			
CGGCCCCCGCAGGCTCTGAACCTGGTGCAGCTCTACAGCC 1600			
1610	1620	1630	1640
ATGTTTCTGAGAACTTGCCACCGTATGCCCCACCTCGGTT 1640			
TCTCAGGCTCCAGGAATCTTTGGCCACTACTGAGACCTTC 1680			
AAACAGCAGAAGGTTAGGATGGCCAATGAGGGCTTTGACC 1720			
CCAGTGTACTGTCTGACCCACTCTATGTTCTGGACCAAGA 1760			
TATAGGGGCTACCTGCCCCCTCACACCTGCCCCGTACAGT 1800			
1810	1820	1830	1840
GCCCTCCTGTCTGGAGACCTTCGAATCTGAAACCTTCCAC 1840			
TTGAGGGAGGGGCTCGGAGGGTACAGGCCACCATGGCTGC 1880			
ACCAGGGAGGGTTTTTCGGGTATCTTTTGTATATGGAGTCA 1920			
TTATTTTGTAAATAAACAGCTGGAGCTTAAAAAAAAAAAAA 1960			
AAA 1998			

Fig. 66B

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mmFATP3 partial.protein

10 20 30 40
ESSESGCSLAWRLAYLAREOPTHTFLIHGAORFSYAEAER 40
ESNRJARAFRLRARGWTGGRRGSGRGSTEEGARVAPPAGDA 80
AARGTTAPPLAPGATVALLLPAGPDFLWIWFGGLAKAGLRT 120
AFVPTALRRGPPLLHCLRSCGASALVLATEFLESLEPDLP 160
LRAMGLHLWATGPETNVAGISNLLSEAADOVDEPVPGYLS 200
210 220 230 240
APONIMDTCLYIFTSGTTGLPKAARISHLKVLCQGFYHL 240
CGVHOEDVIYLALPLYHMSGSLGIVGCLGIGATVVLKPK 280
FSASOFWDDCOKHRVTVFQYIGELCRYLVNPPSKAEFDH 320
KVRLAVGSGLRPDTWERFLRRFGPLQILETYGMTEGNVAT 360
FNYTGRGAVGRASWLYKHIFPFSIRYDVMTEPIRNAQ 400
410 420 430 440
GHCMTTSPGEPGLLVAPVSOOSPFLGYAGAPELAKDKLLK 440
DVFWSGDVFFNTGDLLVCDEOGFLHFHRTGDTIRWKGEN 480
VATTEVAEVLETDLFLQEVNIYGVTVPGEGRAGMAALAL 520
RPPQALNLVQLYSHVSENLPYARPRFLRLOESLATTETF 560
KQOKYRMANEGFDPSVLSPLYVLDODIGAYLPLTPARYS 600
610 620 630 640
ALLSGDLRI. 610

Fig. 67

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mmFATP4 full length.DNA

```
      10      20      30      40
      |      |      |      |
ATGCTGCTTGGAGCCTCTCTGGTGGGGGCGCTACTGTTC 40
CCAAGCTAGTGCTGAAGCTGCCCTGGACCCAGGTGGGATT 80
CTCCCTGTTGCTCCCTGTACTTGGGGTCTGGTGGCTGGCGT 120
TTCATCCGGGTCTTCATCAAGACGGTCAGGAGAGATATCT 160
TTGGTGGCATGGTGTCTCTGAAGGTGAAGACCAAGGTGCG 200

      210      220      230      240
      |      |      |      |
ACGGTACCTTCAGGAGCGGAAGACGGTGCCCTGCTGTTT 240
GCTTCAATGGTACAGCGCCACCCGGACAAGACAGCCCTGA 280
TTTTCGAGGGCACAGACACTCACTGGACCTTCCGCCAGCT 320
GGATGAGTACTCCAGTAGTGTGGCCAACCTCCTGCAGGCC 360
CGGGGCTGGCCTCAGGCAATGTAGTTGCCCTCTTTATGG 400

      410      420      430      440
      |      |      |      |
AAAACCGCAATGAGTTTGTGGGTCTGTGGCTAGGCATGGC 440
CAAGCTGGGCGTGGAGGGGGCTCTCATCAACACCAACCTT 480
AGGCGGGATGCCCTGCGCCACTGTCTTGACACCTCAAAGG 520
CACGAGCTCTCATCTTTGGCAGTGAGATGGCCTCAGCTAT 560
CTGTGAGATCCATGCTAGCCTGGAGCCCACACTCAGCCTC 600

      610      620      630      640
      |      |      |      |
TTCTGCTCTGGATCCTGGGAGCCCAGCACAGTGCCCGTCA 640
GCACAGAGCATCTGGACCTCTTCTGGAAGATGCCCGGAA 680
GCACCTGCCCAGTCACCCAGACAAGGGTTTTACAGATAAG 720
CTCTTCTACATCTACACATCGGGCACCCAGGGGCTACCCA 760
AAGCTGCCATTGTGGTGCACAGCAGGTATTATCGTATGGC 800

      810      820      830      840
      |      |      |      |
TTCCCTGGTGTACTATGGATTCCGCATGCGGCCTGATGAC 840
ATTGTCTATGACTGCCTCCCCCTCTACCACTCAAGCAGGA 880
AACATCGTGGGGATTGGCAGTGCTTACTCCACGGCATGAC 920
TGTGGTGTATCCGGAAGAAGTTCTCAGCCTCCCGGTTCTGG 960
GATGATTGTATCAAGTACAACCTGCACAGTGGTACAGTACA 1000

      1010      1020      1030      1040
      |      |      |      |
TTGGCGAGCTCTGCCGCTACCTCCTGAACCAGCCACCCCG 1040
TGAGGCTGAGTCTCGGCACAAGGTGCGCATGGCACTGGGC 1080
AACGGTCTCCGGCAGTCCATCTGGACCGACTTCTCCAGCC 1120
GTTTCCACATCCCCCAGGTGGCTGAGTTCTATGGGGCCAC 1160
TGAATGCAACTGTAGCCTGGGCAACTTTGACAGCCGGGTG 1200
```

Fig. 68A

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mmFATP4 full length.DNA

1210 1220 1230 1240
GGGGCCTGTGGCTTCAATAGCCGCATCCTGTCCTTTGTGT 1240
ACCCATCCGTTTGGTACGTGTCAATGAGGATACCATGGA 1280
ACTGATCCGGGGACCCGATGGAGTCTGCATTCCCTGTCAA 1320
CCAGGTCAGCCAGGCCAGCTGGTGGGTGCGATCATCCAGC 1360
AGGACCCTCTGCGCCGTTTCGACGGGTACCTCAACCAGGG 1400
1410 1420 1430 1440
TGCCAACAACAAGAAGATTGCTAATGATGTCTTCAAGAAG 1440
GGGGACCAAGCCTACCTCACTGGTGACGTCTGGTGATGG 1480
ATGAGCTGGGTACCTGTACTTCCGAGATCGCACTGGGGA 1520
CACGTTCCGCTGGAAAGGGGAGAATGTATCTACCACTGAG 1560
GTGGAGGGCACACTCAGCCGCCTGCTTCATATGGCAGATG 1600
1610 1620 1630 1640
TGGCAGTTTATGGTGTGAGGTGCCAGGAAGTGAAGGCCG 1640
AGCAGGAATGGCTGCCGTTGCAAGTCCCATCAGCAACTGT 1680
GACCTGGAGAGCTTTGCACAGACCTTGAAAAAGGAGCTGC 1720
CTCTGTATGCCCGCCCCATCTTCCTGCGCTTCTTGCCCTGA 1760
GCTGCACAAGACAGGGACCTTCAAGTTCAGAGACAGAG 1800
1810 1820 1830 1840
TTGCGGAAGGAGGGCTTTGACCCATCTGTTGTGAAAGACC 1840
CGCTGTTCTATCTGGATGCTCGGAAGGGCTGCTACGTTGC 1880
ACTGGACCAGGAGGCCATAACCCGCATCCAGGCAGGCGAG 1920
GAGAAGCTGTGATTTCCCCCTACATCCCTCTGAGGGCCAG 1960
AAGATGCTGGATTTCAGAGCCCTAGCGTCCACCCAGAGGG 2000
2010 2020 2030 2040
TCCTGGGCAATGCCAGACCAAGCTAGCAGGGCCCCGACC 2040
TCCGCCCTTAGGTGCTGATCTCCCCCTCCCCAACTGCCA 2080
AGTGACTCACTGCCGCTTCCCCGACCCTCCAGAGGCTTTC 2120
TGTGAAAGTCTCATCCAAGCTGTGTCTTCTGGTCCAGGCG 2160
TGGCCCCTGGCCCCAGGGTTTCTGATAGGCTCCTTTAGGA 2200
2210 2220 2230 2240
TGGTATCTTGGGTCCAGCGGGCCAGGGTGTGGGAGAGGAG 2240
TCACTAAGATCCCTCCAATCAGAAGGGAGCTTACAAAGGA 2280
ACCAAGGCAAAGCCTGTAGACTCAGGAAGCTAAGTGGCCA 2320
GAGACTATAGTGGCCAGTCATCCCATGTCCACAGAGGATC 2360
TTGGTCCAGAGCTGCCAAAGTGTACCTCTCCCTGCCTGC 2400
2410 2420 2430 2440
ACCTCTGGGGAAAAGAGGACAGCATGTGGCCACTGGGCAC 2440
CTGTCTCAAGAAGTCAGGATCACACACTCAGTCCTTGTTT 2480
CTCCAGGTTCCCTTGTTCTTGTCTCGGGGAGGGAGGGACG 2520
AGTGTCTGTCTGTCTTCTGCCTGTCTGTGAGTCTGTG 2560
TTGCTTCTCCATCTGTCTTAGCCTGAGTGTGGGTGGAACA 2600

Fig. 68B

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mmFATP4 full length.DNA

2610 2620 2630 2640

GGCATGAGGAGAGTGTGGCTCAGGGGCCAATAAACTCTGC 2640
CTTGACTCCTCTTAAAAAAAAAAAAAAAAAAAAAAAAAAAAA 2680
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA 2710

Fig. 68C

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mmFATP4 full length.protein

10 20 30 40
MLLGASLVGALLFSKLVLKLPWTOVGFSLLLLYLGGSGWR 40
FIRVFIKTVRRDIFGGMVLLKVTKVRRYLOERKTVPLLF 80
ASMVORHPDKTALIFEGTDHWTFROLDEYSSSVANFLOA 120
RGLASGNVVALFMENRNEFVGLWLGMAKLGVEAALINTNL 160
RRDALRHCLDTSKARALIFGSEMASAICEIHASLEPTLSL 200
210 220 230 240
FCSGSWEPSTVPVSTEHLDPLLEDAPKHLFSPDKGFTDK 240
LFYIYTSGETTGLPKAAIVVHSRYRMAVLVYGFMRMPDD 280
IVYDCLPLYHSSRKHRGDWOCLLHGMTVIRKKFSASRFW 320
DDCIKYNCTVVQYIGELCRYLLNOPPREAESRHKVRMALG 360
NGLROSJWTDSSRFHIPOVAEFYGATECNCSLGNFDSRV 400
410 420 430 440
GACGFNSRILSFVYPIRLVRVNEDTMELIRGPDGVCIPCO 440
PGPGOLVGR!!OODPLRRFDGYLNOGANNKKIANDVFCK 480
GDOAYLTGQVLVMDLGYLYFRDRTGDTFRWKGENVSTIE 520
VEGTLRLLHMADVAVYGVEVPGTEGRAGMAAVASPI SNC 560
DLESFAOTLKKELPLYARPIFLRFLPELHKTGTGFKFQKTE 600
610 620 630 640
LRKEGFDPSVVKDPLFYLDARKGCYVALDOEAYTRIOAGE 640
EKL. 644

Fig. 69

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mmFATP5 full length.DNA

10 20 30 40
CACTCATCAGAGCTAAGAGAGACTACACGCTCTCATCTAC 40
TTCAGAAAGAGCCAATGCCATGGGTATTTGGAAGAACTA 80
ACCTTACTGCTGTTGCTGCTTCTGCTGGTTGGCCTGGGGC 120
AGCCCCCATGGCCAGCAGCTATGGCTCTGGCCCTGCGTTG 160
GTTCTTGGGAGACCCACATGCCCTGTGCTGCTTGGCTTG 200

210 220 230 240
GCATTGCTGGGCAGACCCTGGATCAGCTCCTGGATGCCCC 240
ACTGGCTGAGCCTGGTAGGAGCAGCTCTTACCTTATTCCT 280
ATTGCCCTCTACAGCCACCCCCAGGGCTACGCTGGCTGCAT 320
AAAGATGTGGCTTTACCTTCAAGATGCTTTTCTATGGCC 360
TAAAGTTCAGGCGACGCCCTAACAACATCCTCCAGAGAC 400

410 420 430 440
CTTTGTGGATGCTTTAGAGCGGCAAGCACTGGCATGGCCT 440
GACCGGGTGGCCTTGGTGTGTACTGGGTCTGAGGGCTCCT 480
CAATCACAATAGCCAGCTGGATGCCAGGTCCTGTCAGGC 520
AGCATGGGTCTTGAAGCAAAGCTGAAGGATGCCGTAATC 560
CAGAACACAAGAGATGCTGCTGCTATCTTAGTTCCTCCCGT 600

610 620 630 640
CCAAGACCATTTCTGCTTTGAGTGTGTTTCTGGGGTTGGC 640
CAAGTTGGGCTGCCCTGTGGCCTGGATCAATCCACACAGC 680
CGAGGGATGCCCTTGCTACACTCTGTACGGAGCTCTGGGG 720
CCAGTGTGCTGATTGTGGATCCAGACCTCCAGGAGAACCT 760
GGAAGAAGTCCTTCCCAAGCTGCTAGCTGAGAACATTAC 800

810 820 830 840
TGCTTCTACCTTGGCCACAGCTCACCCACCCGGGAGTAG 840
AGGCTCTGGGAGCTTCCCTGGATGCTGCACCTTCTGACCC 880
AGTACCTGCCAGCCTTCGAGCTACGATTAAGTGGAAATCT 920
CCTGCCATATTTCATCTTTACTTCAGGGACCACTGGACTCC 960
CAAAGCCAGCCATCTTATCATATGAGCGGGTCATACAAGT 1000

1010 1020 1030 1040
GAGCAACGTGCTGTCTTCTGTGGATGCAGAGCTGATGAT 1040
GTGGTCTATGACGTCCTACCTCTGTACCATACGATAGGGC 1080
TTGTCCITGGATTCCCTGGCTGCTTACAAGTTGGAGCCAC 1120
CTGTGTCTGGCCCCCAAGTTCTCTGCCTCCCGATTCTGG 1160
GCTGAGTGCCGGCAGCATGGCGTAACAGTGAATCTGTATG 1200

Fig. 70A

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mmFATP5 full length.DNA

```
      1210      1220      1230      1240
TGGGTGAAATCCTGCGGTACTTGTGTAACTGTCCTGAGCA 1240
ACCAGAAGACAAGATACATACAGTGCCTTGGCCATGGGA 1280
ACTGGACTTCGGGCAAATGTGTGGAAAACTTCCAGCAAC 1320
GCTTTGGTCCCATTCGGATCTGGGAATTCTACGGATCCAC 1360
AGAGGGCAATGTGGGCTTAATGAACTATGTGGGCCACTGC 1400

      1410      1420      1430      1440
GGGGCTGTGGGAAGGACCAGCTGCATCCTTCGAATGCTGA 1440
CTCCCTTTGAGCTTGTACAGTTCGACATAGAGACAGCAGA 1480
GCTCTGAGGGACAAACAGGGTTTTTGCATTCTGTGGAG 1520
CCAGGAAAGCCAGGACTTCTTTTGACCAAGGTTCGAAAGA 1560
ACCAACCCCTTCTTGGGCTACCGTGGTTCAGGCCGAGTC 1600

      1610      1620      1630      1640
CAATCGGAAACTTGTTCGGAATGTACGACGCTAGGAGAC 1640
CTGTACTTCAACACTGGGGACGTGCTGACCTTGGACCAGG 1680
AAGGCTTCTTCTACTTTCAAGACCGCTTGGTGACACCTT 1720
CCGGTGGAAAGGGCGAAAACGTATCTACTGGAGAGGTGGAG 1760
TGTTGTTTTGCTAGCCTAGACTTCCTAGAGGAAGTCAATG 1800

      1810      1820      1830      1840
TCTATGGTGTGCCCTGTGCCAGGGTGTGAGGGTAAGGTTGG 1840
CATGGCTGCTGTGAAACTGGCTCCTGGGAAGACTTTTGAT 1880
GGGCAGAAGCTATACCAGCATGTCCGCTCCTGGCTCCCTG 1920
CCTATGCCACACCTCATTTTCATCCGTATCCAGGATTCCT 1960
GGAGATCACAAACACCTACAAGCTGGTAAAGTCACGGCTG 2000

      2010      2020      2030      2040
GTGCGTGAGGGTTTTTGATGTGGGGATCATTGCTGACCCCC 2040
TCTACATACTGGACAACAAGGCCAGACCTTCCGGAGTCT 2080
GATGCCAGATGTGTACCAGGCTGTGTGTGAAGGAACCTGG 2120
AATCTCTGACCACCTAGCCAACTGGAAGGCAATCCAAAAG 2160
TGTAGAGATTGACACTAGTCAGCTTACAAAAGTTGTCCGG 2200

      2210      2220      2230      2240
GTTCAGATGCCCATGGCCCAGTAGTACTTAGAGAATAAA 2240
CTTGAATGTGTATACAAAAAAAAAAAAAAAAAAAAAAAAA 2277
```

Fig. 70B

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mmFATP5 full length protein

10 20 30 40
MGIWKKLTLLLLLLLLVGLGPPWPAAMALALRWFLGDPT 40
CLVLLGLALLGRPWISSWMPHWLSLVGAALTFLPLLOPP 80
PGLRWLHKDVAFTFKMLFYGLKFRRRLNKHPPETFVDALE 120
RCALAWPDORVALVCTGSEGSSITNSOLDARSCOAAWVKA 160
KLKDAVIONTRDAAAILVLPSKTIISALSVFLGLAKLGCPV 200
210 220 230 240
AWINPHSRGMPLLSVRSSGASVLIVDPDLQENLEEVLPK 240
LLAENIHCFYLGHSSTPGVEALGASLDAAPSDPVPASLR 280
ATIKWKSPAIFIFTSGTTGLPKPAILSHERVIOVSNVLSF 320
CGCRADDVVYDVLPLYHTIGLVLGFLGCLOVGATCVLAPK 360
FSASRFWAECROHGVTVILYVGEILRYLCNVPEOPEDKIH 400
410 420 430 440
TVRLAMGTGLRANVWKNFOORFGPIRIWEFYGSTEGNVGL 440
MNYVGHCGAVGRTSCILRMLTPFELVOFDIETAELRDKO 480
GFCIPVEPGKPGLLLTKVRKNOPFLGYRGSOAESNRKLVA 520
NVRRVGDLYFNTGDVLTLDQEGFFYFOORLGOTFRWKGEN 560
VSTGEVECVLSSLDLFLEEVNVYGVVPVPGCEGKVGMAAVKL 600
610 620 630 640
APGKTFDGOKLYOHVRSWLPAYATPHFIRIQDSLEITNTY 640
KLVKSRLVREGFDVGIADPLYILDNKAOTFRSLMPDVYD 680
AVCEGTWNL. 690

Fig. 71

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dmFATP partial.DNA

10 20 30 40
GCTCTCTGGGCCTATATCAAGCTGCTGAGGTACACGAAGC 40
GCCATGAGCGGCTCAACTACACGGTGGCGGACGCTCTTCGA 80
ACGAAATGTTAGGCCCATCCGGACAAGGTGGCTGTGGTC 120
AGTGAGACGCAACGCTGGACCTTCCGTCAGGTGAACGAGC 160
ATGCGAACAAGGTGGCCAATGTGCTGCAGGCTCAGGGCTA 200
210 220 230 240
CAAAAAGGGCGATGTGGTGGCCCTGTTGCTGGAGAACC GC 240
GCCGAGTACGTGGCCACCTGGCTGGGTCTCTCCAAGATCG 280
GTGTGATCACACCGCTGATCAACACGAATCTGCGCGGTCC 320
CTCCCTGCTGCACAGCATCACGGTGGCCCATTTGCTCGGCT 360
CTCATTTACGGCGAGGACTTCCTGGAAGCTGTACCCGACG 400
410 420 430 440
TGGCCAAGGATCTGCCAGCGAACCTCACACTCTTCCAGTT 440
CAACAACGAGAACAACAACAGCGAGACGGAAGAACAATA 480
CCGCAGGCCAAGAATCTGAACGCGCTGCTGACCACGGCCA 520
GCTATGAGAAGCCTAACAAGACGCGAGGTTAACCACCACGA 560
CAAGCTGGTCTACATCTACACCTCCGGCACCAAGGATTG 600
610 620 630 640
CCAAAGGCTGCGGTTATCTCTCACTCCCGTTATCTGTTTA 640
TCGCTGCTGGCATCCACTACACCATGGGTTTCCAGGAGGA 680
GGACATCTTCTACACGCCCTTGCCTTTGTACCACACCGCT 720
GGTGGCATTATGTGCATGGGTGAGTCGGTGCTCTTTGGCT 760
CCACGGTCTCCATTTCGAAGAAGTTCTCGGCATCCAATA 800
810 820 830 840
TTTCGCCGACTGCGCCAAGTATAATGCAACTATTGGTCAG 840
TATATCGGTGAGATGGCTCGCTACATTCTAGCTACGAAAC 880
CCTCGGAATACGACCAGAAACACCGAGTGCGTCTGGTCTT 920
TGGAAACGGACTGCGACCGCAGATTGGCCACAGTTTGTG 960
CAGCGCTTCAACATTGCCAAGGTTGGCGAGTTCTACGGCG 1000
1010 1020 1030 1040
CCACCGAGGGTAATGCGAACATCATGAATCATGACAACAC 1040
GGTGGGCGCCATCGGCTTTGTGTGCGGCATCCTGCCCCAAG 1080
ATCTACCCAATCTCGATCATTCGCGCCGATCCGGACACCG 1120
GAGAGCCCATAGAGATAGGAATGGCCTATGCCAACTGTG 1160
CGTCCCCAACGAGCCAGGCGTATTCATCGGCAAGATCGTC 1200

Fig. 72A

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dmFATP partial.DNA

```

      1210      1220      1230      1240
      | | | | | | | | | | | | | | | |
AAAGGAAATCCTTCTCGCGAATTCCTCGGATACGTCGATG 1240
AAAAGGCCTCCGCGAAGAAGATTGTTAAGGATGTGTTCAA 1280
GCATGGCGATATGGCTTTCATCTCCGGAGATCTGCTGGTT 1320
GCCGACGAGAAGGGTTATCTGTACTTCAAGGATCGCACCG 1360
GTGACACCTTCCGCTGGAAGGGCGAGAATGTTTCCACCAG 1400

      1410      1420      1430      1440
      | | | | | | | | | | | | | | | |
CGAGGTGGAGGCGCAAGTCAGCAATGTGGCCGGTTACAAG 1440
GATACCGTCGTTTACGGCGTAACCATTCGCGACACCGAGG 1480
GAAGGGCCGGCATGGCCGCCATCTATGATCCGGAGCGAGA 1520
ATTGGACCTCGACGTCTTCGCCGCTAGCTTGGCCAAGGTG 1560
CTGCCCGCGTACGCTCGTCCCCAGATCATTGATTGCTCA 1600

      1610      1620      1630      1640
      | | | | | | | | | | | | | | | |
CCAAGGTGGACCTGACTGGAACCTTTAAGCTGCGCAAGGT 1640
AGACCTGCAGAAGGAGGGCTACGATCCGAACGCGATCAAG 1680
GACGCGCTGTACTACCAGACTTCCAAGGGTCGGTACGAGC 1720
TGCTCAGCCCCAGGTTTACGACCAGGTGCAGCGCAACGA 1760
AATCCGCTTCTAAGAGCTGCAATAGAGTTGTGTCTGAACC 1800

      1810      1820      1830      1840
      | | | | | | | | | | | | | | | |
TTGCCTTTTGCCCAATATGCTGTTAATTAGTTTGTAAAGGC 1840
TAAGTGTAGTAGAGGAAAATCGGGGGAAATCGGCAGCAAA 1880
GATCATTCAGCCTAGGAGAGATGCATCCGAAGCACATTTT 1920
CATGTCAACAATGCACTTTTGTATATCGTAAGCATATATA 1960
TATCGTATATCGTAAACGTAGTTGTATCTGCATTTGTGTA 2000

      2010      2020      2030      2040
      | | | | | | | | | | | | | | | |
GATGATAGCCTCTATACGCATTTCAATTGTTTTAGCGT 2040
GCTAAAGAACCTTGTAAATGCAATTTTCAAGCTATTGTTA 2080
GTCAGTTTTAGTGGCATTACACTTCCATTCTCGTTGCGT 2120
TTCGTTTTTGCTGTACATATGAGAAGCTCTGATGTTTTT 2160
GTATCAAATAAAGTTTTTTCCTTCACCACGGACCACGTGA 2200

      2210      2220      2230      2240
      | | | | | | | | | | | | | | | |
AAAAAAAAAAAAAAAAAAAAA 2221

```

Fig. 72B

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dmFATP partial.protein

10 20 30 40
ALWAYIKLLRYTKRHERLNYTVADVFERNVQAHPOKVAVV 40
SETQRWTFROVNEHANKVANVLOAGYKKGOVVALLENR 80
AEYVATWLGLSKIGVITPLINTNLRGPSLLHSITVAHCSA 120
LIYGEDFLEAVTOVAKDLPANLTLFQFNENNNNSETEKNI 160
POAKNLNALLTTASYEKPNTQVNHDKLVYIYTS GTTGL 200
210 220 230 240
PKAAVISHSRYLFIAAGIHYTMGFQEEIDFYTPLPLYHTA 240
GGIMCMGOSVLFGSTVSIRKKFSASNYFADCAKYNATIGO 280
YIGEMARYILATKPSEYDQKHRVRLVFGNGLRPQIWPOFV 320
ORFNIKVGFEFYGATEGNANIMNHDNTVGAIGFVSRILPK 360
IYPISIIIRADPDTGEPIDRNLGLCOLCAPNEPGVFIGKIV 400
410 420 430 440
KGNPSREFLGYVDEKASAKKIVKDVFKHGDMAFISGOLLV 440
ADEKGYLYFKDRTGDTFRWKGENYSTSEVEAOVSNVAGYK 480
DTVVYGVYIPHTEGRAGMAAIYDPERELDLVDFAASLAKV 520
LPAYARPOIIRLLTKVDLTGTFKLKRVLDLOKEGYDPNAIK 560
DALYYQTSKGRYELLTPQYDQVORNEIRF 590

Fig. 73

drFATP partial.DNA 91/117

10 20 30 40
AGTGTAGATACACAGGAACGTTTAAAATCCAGAAGACCA 40
GACTGCAAAGGGAAGGATACGATCCACGGCTCACAACCTGA 80
CCAGATCTACTTCCTAAACTCCAGAGCAGGGCGTTACGAG 120
CTTGTCAACGAGGAGCTGTACAATGCATTTGAACAAGGGC 160
AGGATTTCCCTTT 173

Fig. 74

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drFATP partial.protein

10 20 30 40
SVDTTGTFKIQKTRLOREGYDPRLTTDQIYFLNSRAGRYE 40
LVNEELYNAFEQGGDFP 57

Fig. 75

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ceFATPa coding only.DNA

```

      10      20      30      40
      +      +      +      +
ATGAAGCTGGAGGAGCTTGTGACAGTTATGCTTCTCACAG 40
TGGCTGTCATTGCTCAGAATCTTCCGATTGGAGTAATATT 80
GGCTGGAGTTCTTATTTTATACATCACAGTGGTTCATGGA 120
GATTTCAATTATAGAAGTTATCTTACGTTGAATAGGGATT 160
TAACAGGATTGGCTCTAATTATTGAAGTCAAATCGACCT 200
      210      220      230      240
      +      +      +      +
ATGGTGGAGGTTGCATCAGAATAAAGGAATCCATGAACTG 240
TTTTTGGATATTGTGAAAAAGAATCCAAATAAGCCGGCGA 280
TGATTGACATCGAGACGAATACAACAGAAACATACGCAGA 320
GTTCAATGCACATTGTAATAGATATGCCAATTATTTCCAG 360
GGTCTTGGCTATCGATCCGGAGACGTTGTGCGCTTGTACA 400
      410      420      430      440
      +      +      +      +
TGGAGAACTCGGTCGAGTTTGTGGCCGCGTGGATGGGACT 440
CGCAAAAATCGGAGTTGTAACGGCTTGGATCAACTCGAAT 480
TTGAAAAGAGAGCAACTTGTTCATTGTATCACTGCGAGCA 520
AGACAAAGGCGATTATCACAAGTGTAACACTTCAGAATAT 560
TATGCTTGATGCTATCGATCAGAAGCTGTTTGATGTTGAG 600
      610      620      630      640
      +      +      +      +
GGAATTGAGGTTTACTCTGTCTGGAGAGCCCAAGAAGAATT 640
CTGGATTCAAGAATCTCAAGAAGAAGTTGGATGCTCAAAT 680
TACTACGGAACCAAGACCCCTTGACATAGTAGATTTTAAA 720
AGTATTCTTTGCTTCATCTATACAAGTGGTACTACTGGAA 760
TGCCAAAAGCCGCTGTCATGAAGCACTTCAGATATTACTC 800
      810      820      830      840
      +      +      +      +
GATTGCCGTTGGAGCCGCAAAATCATTCCGAATCCGCCCT 840
TCTGATCGTATGTACGTCTCGATGCCAATTTATCACACTG 880
CAGCTGGAATTCTTGGAGTTGGGCAAGCTCTGTTGGGTGG 920
ATCATCGTGTGTCATTAGAAAAAAATCTCGGCTAGCAAC 960
TTTTGGAGGGATTGTGTAAGTATGATTGTACAGTTTCAC 1000
      1010      1020      1030      1040
      +      +      +      +
AATACATTGGAGAGATTTGTCTGGTACTTGTGGCTCAGCC 1040
AGTTGTGGAAGAGGAATCCAGGCATAGAATGAGATTGTTG 1080
GTTGGAAACGGACTCCGTGCTGAAATCTGGCAACCATTTG 1120
TAGATCGATTCCGTGTCAGAATTGGAGAACTTTATGGTTC 1160
AACTGAAGGAACCTCATCTCTCGTGAACATTGACGGACAT 1200

```

Fig. 7A

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ceFATPa coding only.DNA

```
      1210      1220      1230      1240
      | | | | | | | | | | | | | | | | | |
GTCGGAGCTTGCGGATTCTTGCCAATATCCCCATTAACAA 1240
AGAAAATGCATCCGGTTCGATTAATTAAGGTTGATGATGT 1280
CACTGGAGAAGCAATCCGAAC TTCCGATGGACTTTGCATT 1320
GCATGTAATCCAGGAGAGTCTGGAGCAATGGTGTGCGACGA 1360
TCAGAAAAAATAATCCATTATTGCAATTCGAGGGATATCT 1400
      1410      1420      1430      1440
      | | | | | | | | | | | | | | | | | |
GAATAAGAAGGAAACGAATAAAAAGATTATCAGAGATGTC 1440
TTCGCAAAGGGAGATAGTTGCTTTTTGACTGGAGATCTTC 1480
TTCATTGGGATCGTCTTGTTATGTATATTTCAAGGATCG 1520
TACTGGAGATACTTTCCGTTGGAAGGGAGAGAATGTGTGCG 1560
ACTACTGAAGTCGAGGCAATTCTTCATCCAATTACTGGAT 1600
      1610      1620      1630      1640
      | | | | | | | | | | | | | | | | | |
TGTCTGATGCAACTGTTTATGGTGTAGAGGTTCTCTCAAAG 1640
AGAGGGAAGAGTTGGAATGGCGTCAGTTGTTGAGTTGTA 1680
TCGCATGAGGAAGATGAAACTCAATTTGTTTCATAGAGTTG 1720
GAGCAAGACTTGCCCTCTTCGCTTACCAGCTACGCGATTCC 1760
TCAGTTTATGCGAATTTGTCAGGATGTTGAGAAAAACAGGT 1800
      1810      1820      1830      1840
      | | | | | | | | | | | | | | | | | |
ACATTCAAAC TTGTGAAGACGAATCTACAACGATTAGGTA 1840
TCATGGATGCTCCTTCAGATTCAATTTACATCTACAATTC 1880
TGAAAATCGCAATTTTGTGCCGTTTCGACAATGATTTGAGG 1920
TGCAAGGTCTCACTGGGAAGTTATCCATTTTAA 1953
```

Fig. 76B

95/117

ceFATPa coding only.protein

10 20 30 40
MKLEELVTVMLLTVAVIAONLPIGVILAGVLILYITVVHG 40
DFIYRSYLTNRLDTGLALIEVKIDLWRLHONKGIHEL 80
FLDIVKKNPKNPAMIDIEETNTTETIAEFNAHCNRYANYFO 120
GLGYRSGDVVALYMENSVEFVAAWMGLAKIGVVTAWINSN 160
LKREQLVHCITASKTKAIIITSVTLQNIMLDAIDOKLFOVE 200
210 220 230 240
GIEVYSVGEPKKNSGFKNLKKKLDAQITTEPKTLDIVDFK 240
SILCFIYTSGTTGMPKAAVMKHFYYSIAVGAAKSFGIRP 280
SDRMVVSMPYHTAAGILGVGOALLGGSSCVIRKKFSASN 320
FWRDCVKYDCTVSQYIGEICRYLLAQPVEEESRHRMRL 360
VGNGLRAEIWOPFVDRFRVRIGELYGSTEGTSSLVNIDGH 400
410 420 430 440
VGACGFLPISPLTKKMHPVRLIKVDDVTGEAIRTSGLCI 440
ACNPGESGAMVSTIRKNNPLLOFEGYLNKKETNKKIIRDV 480
FAKGDSCFLTGDLLHWDRLGYVYFKDRTGDTFRWKGENVS 520
TTEVEAILHPITGLSDATVYGVEVPQREGRVGMASVVRVV 560
SHEEDETQFVHRVGARLASSLTSYAIPQFMRICQDVEKTG 600
610 620 630 640
TFKLVKTNLQRLGIMDAPSDSIYIYNSENRRNFVFPDNDLR 640
CKVSLGSYPF. 651

Fig. 77

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ceFATPb coding only.DNA

10 20 30 40
ATGAGGGAAATGCCGGACAGTCCCAAGTTTGCGTTAGTCA 40
CGTTTGTGTGTATGCAGTGGTTTTGTACAATGTCAACAG 80
CGTTTTCTGGAAATTTGTATTCATCGGATATGTTGATTT 120
AGGCTGCTTCGCACTGATTTTGAAGAAGAGCACTTGCCA 160
CGTTACCTAGAGATTTTGCGGGACTGAAGCTCTTAATATC 200
210 220 230 240
GGTTAAGTCGACAATTCGTGGCTTGTTCAGAAAGATCGC 240
CCAATTCATGAAATCTTTTGAATCAGGTGAAACAGCATC 280
CAAAACAAAGTGGCGATTATTGAAATTGAAAGTGGTAGGCA 320
GTTGACGTATCAAGAATTGAATGCGTTAGCTAATCAGTAT 360
GCTAACCTTTACGTGAGTGAAGGTTACAAAATGGGCGACG 400
410 420 430 440
TTGTCGCTTTGTTTATGGAAAATAGCATCGACTTCTTTGC 440
AATTTGGCTGGGACTTTCCAAGATTGGAGTCGTGTCGGCG 480
TTCATCAACTCAAACCTTGAAGTTGGAGCCATTGGCACATT 520
CGATTAATGTTTTCGAAGTGCAAATCATGCATTACCAATAT 560
CAATCTGTTGCCGATGTTCAAAGCCGCTCGTGAAAAGAAT 600
610 620 630 640
CTGATCAGTGACGAGATCCACGTGTTTCTGGCTGGAATC 640
AGGTTGATGGACGTATAGAAGTCTTCAGCAAGATCTCCA 680
TCTTTTCTCTGAGGATGAACCTCCAGTTATAGACGGACTC 720
AATTTTAGAAGCGTTCTGTGTTATATTTACACTTCCGGTA 760
CTACCGGAAATCCAAAGCCAGCCGTCATTAACACTTCCG 800
810 820 830 840
TTACTTCTGGATTGCGATGGGAGCAGGAAAAGCATTGGA 840
ATTAATAAGTCAGACGTTGTGTACATTACGATGCCAATGT 880
ATCACTCTGCCGCCGGTATCATGGGTATTGGATCATTAA 920
TGCATTGCGGTTCGACCGCTGTTATTAGGAAAAAGTTTTCG 960
GCAAGCAACTTCTGGAAAGATTGCGTCAAGTACAACGTCA 1000
1010 1020 1030 1040
CAGCGACACAGTACATTGGAGAAATCTGCAGGTATCTTCT 1040
GGCAGCGAATCCATGTCTGAAGAGAAACAACAACGTG 1080
CGATTGATGTGGGAAATGGTTTGAGAGGACAAATTTGGA 1120
AAGAGTTTGTAGGAAGATTTGGAATTAAGAAAATTGGAGA 1160
GTTGTACGGCTCAACAGAAGGAAACTCCAATATTGTTAAC 1200

Fig. 78A

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ceFATPb coding only.DNA

1210	1220	1230	1240
GTGGATAACCATGTTGGAGCTTGTGGATTTCATGCCAATTT 1240			
ATCCCCATATTGGATCCCTCTACCCAGTTCGACTTATTAA 1280			
GGTTGATAGAGCCACTGGAGAGCTTGAACGTGATAAGAAC 1320			
GGACTCTGTGTGCCGTGTGTGCCTGGTGAAACTGGGGAAA 1360			
TGGTTGGCGTTATCAAGGAGAAAGATATTCTTCTAAAGTT 1400			
1410	1420	1430	1440
CGAAGGATATGTCAGCGAAGGGGATACTGCAAAGAAAATC 1440			
TACAGAGATGTGTTCAAGCATGGAGATAAGGTGTTTGCAA 1480			
GTGGAGATATTCTTCATTGGGATGATCTTGGATACTTGTA 1520			
CTTTGTGGACCGTTGTGGAGACACTTTCCGTTGGAAAGGG 1560			
GAGAACGTGTCAACTACTGAAGTTGAGGGAATTCTTCAGC 1600			
1610	1620	1630	1640
CTGTGATGGATGTGGAAGATGCAACTGTTTATGGAGTCAC 1640			
TGTCGGTAAAATGGAGGGGCGTGCCGGAATGGCTGGTATT 1680			
GTCGTCAAGGATGGAACGGATGTTGAGAAATTCATCGCCG 1720			
ATATTACTTCTCGACTGACCGAAAAATCTGGCGTCTTACGC 1760			
AATCCCTGTTTTTCATTTCGGCTGTGCAAGGAAGTTGATCGA 1800			
1810	1820	1830	1840
ACCGGAACCTTCAAACCTCAAGAAGACTGATCTTCAAAAAC 1840			
AAGGTTACGACCTGGTTGCTTGTAAGGAGACCCAATTTA 1880			
CTACTGGTCAGCTGCAGAAAAATCCTACAAACCACTGACT 1920			
GACAAAATGCAACAGGATATTGACACTGGTGTATTATGATC 1960			
GCATTTAA 1968			

Fig. 78B

98/117

ceFATPb coding only.protein

10 20 30 40
MREMPOSPKFALVTFVVYAVVLYNVNSVFWKVFVIGYVVF 40
RLLRTOFGRRALATLPRDFAGLKLLISVKSTIRGLFKKDR 80
PIHEIFLNQVKOHPNKVAIIEIESGROLTYOELNALANQY 120
ANLYVSEGYKMGDVVALFMENSIDFFAIWLGLSKIGVSA 160
FINSNLKLEPLAHSINVSKCKSCITNINLLPMFKAAREKN 200

210 220 230 240
LISDEIHVFLAGTOVDGRHRSLODDLHLFSEDEPPVIDGL 240
NFRSVLCYIYTSGTTGNPKPAVIKHFRYFWIAMGAGKAFG 280
INKSDVVYITMPMYHSAAGIMGIGSLIAFGSTAVIRKKFS 320
ASNFWKDCVKYNVTATQYIGEICRYLLAANPCPEEKOHNV 360
RLMWGNGLRGQIWKEFVGRFGIKKIGELYGSTEGNSNIVN 400

410 420 430 440
VDNHVGACGFMPYIYPHIGSLYPVRLIKVD RATGELERDKN 440
GLCVPVCPGETGEMVGVIKEKDILLKFEGYVSEGDTAKKI 480
YRDVFKHGDVVFASGDIHWD DLGYLYFVDRCGDTFRWKG 520
ENVSTTEVEGILQPVMDVEDATVYGVTVGKMEGRAGMAGI 560
VVKDGT DVEKFIADITSRLTENLASYAIPVFIRLCKEVDR 600

610 620 630 640
TGTFKLKKTDLQKQGYDLVACKGDPYIYW SAAEKSYKPLT 640
DKMOODIDTGYYDRI. 656

Fig. 79

99/117

chFATP coding only.DNA

10 20 30 40
ATGGCGTGTATGCATCAGGCTCAGCTATACAATGATCTAG 40
AGGAATTGCTAACTGGTCCATCAGTACCCATCGTTGCTGG 80
AGCTGCTGGAGCTGCAGCTCTCACTGCCTACATTAACGCC 120
AAATACCACATAGCCCATGATCTCAAGACCCTCGGTGGTG 160
GATTGACACAATCGTCCGAAGCGATTGATTTATAAACCG 200
210 220 230 240
CCGCGTCGCACAAAAGCGCGTCCTCACGCACCACATCTTC 240
CAGGAGCAGGTCCAAAAACAATCAAATCATCCCTTTCTTA 280
TCTTTGAGGGCAAGACATGGTCTTACAAGGAGTTCTCTGA 320
GGCATAACGAGGGTCCGGAAGTGGCTGATTGATGAGCTG 360
GACGTACAAGTAGGGGAGATGGTCGCAATTGATGGCGGAA 400
410 420 430 440
ATAGTGCAGAGCACCTGATGCTTTGGCTTGCACTTGATGC 440
AATCGGTCCGGCTACGAGTTTTTTGAACTGGAACCTGACA 480
GGGGCAGGGTTAATTCATTGCATAAAGCTATGCGAATGTC 520
GATTCGTTATCGCAGACATCGATATTAAAGCGAACATTGA 560
ACCGTGCCGTGGCGAACTGGAGGAGACGGGCATCAACATT 600
610 620 630 640
CACTACTATGACCCATCCTTCATCTCATCGCTACCGAATA 640
ACACGCCAATTCCTGACAGCCGCACTGAGAACATTGAATT 680
AGATTCACTACGAGGACTGATATACACATCTGGAACCACT 720
GGTCTACCTAAAGGCGTGTTTATAAGCACTGGCCGCGAGC 760
TTAGGACTGACTGGTCGATTTCAAAGTATCTAAATCTCAA 800
810 820 830 840
GCCCCAGGATCGAATGTATACATGTATGCCGCTCTACCAT 840
GCCGCTGCACACAGCCTCTGTACAGCATCAGTTATTCATG 880
GTGGAGGTACCGTGGTATTGAGCAGGAAATTCACACAA 920
GAAGTTCTGGCCTGAAGTTGTGGCTTCGGAAGCAAATATC 960
ATTCAGTACGTTGGTGAATTAGGTCGATATCTCCTGAATG 1000
1010 1020 1030 1040
GTCCAAAGAGTCCTTACGACAGGGCCCATAAAGTCCAGAT 1040
GGCGTGGGGCAATGGCATGCGTCCAGACGTGTGGGAAGCG 1080
TTTCGTGAACGCTTCAACATACCAATTATTCATGAGCTCT 1120
ATGCCGCAACCGATGGGCTCGGGTCAATGACCAATCGTAA 1160
CGCGGGCCCTTTTACAGCAAACGTATTGCGCTGCGAGGG 1200

Fig. 80A

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chFATP coding only.DNA

1210	1220	1230	1240
CTGATCTGGCACTGGAAATTT	CGAAATCAGGAAGTGCTGG	1240	
TCAAGATGGATCTCGATACTGATGAGATCATGAGAGATCG	1280		
CAATGGGTTTTCGATACGATGCGCTGTCAATGAACCTGGA	1320		
CAGATGCTTTTTCGGCTGACACCCGAAACTCTGGCTGGTG	1360		
CACCAAGCTACTACAACAACGAAACGGCCACACAGAGCAG	1400		
1410	1420	1430	1440
GCGGATTACAGATGTGTTTCAAAGGGTGACCTGTGGTTC	1440		
AAGTCCGGTGACATGCTACGGCAAGACGCCGAAGGCCGCG	1480		
TCTACTTTGTGCGACTAGGCGATACGTTCCGCTGGAA	1520		
ATCCGAAAACGTTTCTACCAATGAAGTCGCGGACGTGATG	1560		
GGCACATTTCTCAGATTGCTGAAACGAATGTATACGGTG	1600		
1610	1620	1630	1640
TCCTTGTGCCGGGTAACGATGGTTCGAGTGCGCAGCCTCAA	1640		
TTGTTCATGGCAGACGGCGTGACAGAGTCGACATTCGCTTC	1680		
GCTGCCCTTGCAAAGCACGCCCAGATCGGTTACCGGGTT	1720		
ATGCTGTACCACTGTTTCTGAGGGTAACTCCAGCACTTGA	1760		
ATATACGGGCACATTAAAGATTTCAGAAAGGACGCCTCAAG	1800		
1810	1820	1830	1840
CAGGAAGGTATAGACCCAGATAAGATTTCCGGCGAAGATA	1840		
AGTTATACTGGCTGCCGCCTGGTAGCGATATATTTACC	1880		
ATTTGGAAAGATGGAGTGGCAGGGAATTGTAGATAAGCGT	1920		
ATACGGCTGTGA	1932		

Fig. 80B

101/117

chFATP coding only.protein

10 20 30 40
MACMHQAOLYNDLEELLTGPSVPIVAGAAGAAALTAYINA 40
KYHIAHDLKTLGGGLTOSSEAIIDFINRRVAOKRVLTHHIF 80
OEOVKOSNHPFLIFEGKTWSYKEFSEAYTRVANWLIDEL 120
DVOVGEMVAIDGGNSAEHMLWLALDAIGAATSFLNWNLT 160
GAGLIHCIKLCECRFVIADIDIKANIEPCERGELEETGINI 200
210 220 230 240
HYYDPSFISSLPNNTPIPDSTRTENIELDSVRGLIYTS GTT 240
GLPKGVIISTGRELRTOWSISKYLNKPTDRMYTCMP LYH 280
AAAHSLCTASVIHGGGTVVLSRKFSHKKFWPEVVASEANI 320
IOYVGELGRYLLNGPKSPYDRAHKVOMAWGNGMRPOVWEA 360
FRERFNIPIIHELYAATDGLGSMTNRNAGPFTANCIALRG 400
410 420 430 440
LIWHWKFRNQEVLVKMDLOTDEIMRDRNGFAIRCAVNEPG 440
OMLFRLTPETLAGAPSYNNETATOSRRITOVFOKGDLWF 480
KSGDMLRODAEGRVYFVDRLGDTFRWKSENVSTNEVADVM 520
GTFPOIAETNVYGVLPVGNDRVRSLNCHGRRRORVDIRF 560
AALAKHARDRLPGYAVPLFLRVTPALEYTGTLKIOKGR LK 600
610 620 630 640
QEGIDPKISGEDKLYWLPPGSDIYLPFGKMEWQGI VDKR 640
IRL 643

Fig. 81

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aspergillus partial.DNA

10 20 30 40
CTTTACCATTCATCAGCTTCATTCTGCATTTTGTAGCTTGA 40
CGGCAGCCGGGTCTACGCTGATCATCGGCCGCAAGTTCTC 80
CGCGAGAACTTCATAAAGGAAGCGCGCGAGAACGACGCC 120
ACGGTCATCCAGTACGTGGGTGAGACCTTGCGATATCTGC 160
TCGCCACCCCGGTGAAACCGATCCAGTTACTGGCGAAGA 200
210 220 230 240
CCTGGACAAAAAGCACAAATATTCGAGCAGTATACGGCAAC 240
GGGCTACGGCCGGATATCTGGAACCGCTTCAAGGAGCGCT 280
TCAACGTGCCGACGGTTGCCGAATTTTATGCTGCAACCGA 320
GAGCCCAGGCGGAACATGGAACATTTCAACAAATGACTTC 360
ACTGCCGGAGCCATTGGGCACACTGGCGTGCTTAGTGGAT 400
410 420 430 440
GGCTTCTTGGACGCGGCCTTACTATTGTGCGAGGTGGACCA 440
GGAATCACAGGAACCATGGCGCGATCCCCAAACCGGGTTC 480
TGCAAGCCGGTCCCGCGAGGCGAAGCAGGCGAGCTCCTGT 520
ATGCCATTGATCCGGCCGACCCGGGCGAGACCTTCCAGGG 560
CTACTACGCAACTCCTTTAGAGCACACTGGCGGCCG 597

Fig. 82

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aspergillus partial.protein

10 20 30 40

LYHSSASFCIFSLTAAGSTLIIGRKFSARNFIKEAREND 40
TVIOYVGETLRYLLATPGETDPVTGEDLDKKHNIRAVYGN 80
GLRPDIWNRKERNVPTVAEFYAATESPGGTWNYSTNDF 120
TAGAIGHTGYLSGWLLGRGLTIVEVDOESQEPWRDPOTGF 160
CKPVPRGEAGELLYAIDPADPGETFOGYRNSFRAHWRP 199

Fig. 83

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mgFATP partial.DNA

10 20 30 40
GCAAAGGCCGACGCGTGGCTGCGGACGGGTAACGTGATCA 40
GGGCGGACAACGAAGGGCGACTCTTCTTCCACGACCGGAT 80
CGGAGACACGTTCGATGGAAGGGAGAGACNGTCAGCACA 120
CAAGAGGTCAGTTTGGTGCTCGGACGACACGACTCAATCA 160
AGGAGGCCAACGTGTACGGCGTGACGGTGCCGAACCACGA 200
210 220 230 240
CGGGCGGGCCGGCTGCGCTGCGCTCACGCTATCAGACGCT 240
CTGGCGACTGAAAAGAAGCTGGGCGATGAGCTGCTAAAGG 280
GATTGGCTACTCACTCGTCGACTTCGCTTCCCAAGTTTGC 320
GGTGCCGCAGTTCCTACGGGTGGTGCGCGGCGAGATGCAG 360
TCAACGGGCACCAACAAGCAACAGAAGCACGACCTGAGGG 400
410 420 430 440
TGCAGGGTGTAGAGCCGGGCAAGGTGGGCGTAGACGAGGT 440
GTACTGGTTGCGGGGAGGGACATATGTACCATTTCGAACA 480
GAGGATTGGGATGGGTTGAAGAAGGTCTTGTGAAGTTGT 520
GA 522

Fig. 84

105/117

mqFATP partial.protein

10 20 30 40

AKADAWLRTGNVIRADNEGRLFFHDIRIGDTRWKGETVST 40
QEVSLVLGRHDSIKEANVYGVTVPNHDGRAGCAALTLSDA 80
LATEKKLGDELLKGLATHSSTSLPKFAVPOFLRVVRGEMO 120
STGTNKOOKHDLRVQGVPEPGKVGVDVYWLRRGGTYVPFGT 160
EDWDGLKKGLVKL 173

Fig. 85

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scFATP coding only.DNA

10 20 30 40
ATGTCTCCCATACAGGTTGTTGTCTTTGCCTTGTC AAGGA 40
TTTTCTGCTATTATTTCAGACTTATCAAGCTAATTATAAC 80
CCCTATCCAGAAATCACTGGGTTATCTATTTGGTAATTAT 120
TTTGATGAATTAGACCGTAAATATAGATAAAGGAGGATT 160
GGTATATTATTCCTTACTTTTTGAAAAGCGTGTGTTGTTA 200
210 220 230 240
TATCATTGATGTGAGAAGACATAGGTTTCAAACTGGTAC 240
TTATTTATTAACAGGTCCAACAAAATGGTGACCATTAG 280
CGATTAGTTACACCCGTCCCATGGCCGAAAAGGGAGAATT 320
TCAACTCGAAACCTTTACGTATATTGAACTTATAACATA 360
GTGTTGAGATTGTCATATTTTGCATTTTGATTATAACG 400
410 420 430 440
TTCAGGCCGGTGACTACGTGGCAATCGATTGTTACTAATAA 440
ACCTCTTTTCGTATTTTATGGCTTTCTTTGTGGAACATT 480
GGGGCTATTCCAGCTTTTTTAACTATAATACTAAAGGCA 520
CTCCGCTGGTTCACTCCCTAAAGATTTCGAATATTACGCA 560
GGTATTTATTGACCCTGATGCCAGTAATCCGATCAGAGAA 600
610 620 630 640
TCGGAAGAAGAAATCAAAAACGCACTTCTGATGTTAAAT 640
TAACTATCTTGAAGAACAAGACTTAATGCATGAACTTT 680
AAATTCGCAATCACCAGGAAATCTTACAACAAGACAACGTT 720
AGGACACCACTAGGCTTGACCGATTTTAAACCCTCTATGT 760
TAATTTATACATCTGGAACCACTGGTTTGCCTAAATCCGC 800
810 820 830 840
TATTATGTCTTGGAGAAAATCCTCCGTAGGTTGTCAAGTT 840
TTTGGTCATGTTTTACATATGACTAATGAAAGCACTGTGT 880
TCACAGCCATGCCATTGTTCCATTCACTGCTGCCTTATT 920
AGGTGCGTGCGCCATTCTATCTCACGGTGGTTGCCTTGCG 960
TTATCGCATAAATTTCTGCCAGTACATTTTGAAGCAAG 1000
1010 1020 1030 1040
TTTATTTAACAGGAGCCACGCACATCCAATATGTCGGAGA 1040
AGTCTGTAGATACCTGTTACATACGCCAATTTCTAAGTAT 1080
GAAAAGATGCATAAGGTGAAGGTTGCTTATGGTAACGGGC 1120
TGAGACCTGACATCTGGCAGGACTTCAGGAAGAGGTTCAA 1160
CATAGAAGTTATTGGTGAATTCTATGCCGCAACTGAAGCT 1200

Fig. 86A

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scFATP coding only.DNA

```
      1210      1220      1230      1240
      | | | | | | | | | | | | | | | | | |
CCTTTTGCTACAACCTACCTTCCAGAAAGGTGACTTTGGAA 1240
TTGGCGCATGTAGGAACCTATGGTACTATAATTCAATGGTT 1280
TTTGTCAATCCAACAACATTGGTAAGGATGGACCCAAAT 1320
GACGATTCGGTTATATATAGAAATTCCAAGGGTTTCTGCG 1360
AAGTGGCCCCCTGTTGGCGAACCAGGAGAAATGTTAATGAG 1400

      1410      1420      1430      1440
      | | | | | | | | | | | | | | | | | |
AATCTTTTTCCCTAAAAAACCAGAAACATCTTTTCAAGGT 1440
TATCTTGGTAATGCCAAGGAAACAAAGTCCAAAGTTGTGA 1480
GGGATGTCTTCAGACGTGGCGATGCTTGGTATAGATGTGG 1520
AGATTTATTAAGCGGACGAATATGGATTATGGTATTTTC 1560
CTTGATAGAATGGGTGATACTTTTCAGATGGAAATCTGAAA 1600

      1610      1620      1630      1640
      | | | | | | | | | | | | | | | | | |
ATGTTTCCACTACTGAAGTAGAAGATCAGTTGACGGCCAG 1640
TAACAAAGAACAATATGCACAAGTTCTAGTTGTTGGTATT 1680
AAAGTACCTAAATATGAAGGTAGAGCTGGTTTTGCAGTTA 1720
TTAAACTAACTGACAACCTCTTTGACATCACTGCAAAGAC 1760
CAAATTATTAATGATTCTTTGAGCCGGTTAAATCTACCG 1800

      1810      1820      1830      1840
      | | | | | | | | | | | | | | | | | |
TCTTATGCTATGCCCCTATTTGTTAAATTTGTTGATGAAA 1840
TTAAATGACAGATAACCTCATAAAATTTGA 1872
```

Fig. 86B

108/117

scFATP coding only.protein

10 20 30 40
MSP IOVVVFALSRIFLLLFRLIKLIITPIOKSLGYLFGNY 40
FDELD RKYRYKEDWYIIPYFLKSVFCYIIDVRRHRFONWY 80
LFIKOVQONGDHLAISYTRPMAEKGEFQLETFTYIETYN 120
VLRLSHILHFDYNVOAGDYVAIDCTNKPLFVFLWLSLWN 160
GAIPAFLNYNTKGTPLVHSLKISNITOVFIOPDASNPIRE 200
210 220 230 240
SEEEIKNALPDVKLNYLEEODLMHELLNSOSPEFLOQDNV 240
RTPLGLTDFKPSMLIYTSGTTGLPKSAIMSWRKSSVGC OV 280
FGHVLHMTNESTVFTAMPLFHSTAALLGACAILSHGGCLA 320
LSHKFSASTFWKQVYLTGATHIOYVGEVCRYLLHTPI SKY 360
EKMHKVKVAYGNGLRPDIWODFRKRFNIEVIGEFYAATEA 400
410 420 430 440
PFATTTFOKGDFGIGACRNYGTIIOWFLSFOOTLVRMDPN 440
DDSVIYRNSKGFCEVAPVGEPGEMLMRIFFPKKPETSFOG 480
YLGNAKETKSKVVRDVFRRGDAWYRCGDLLKADEYGLWYF 520
LORMGDTFRWKSENVSTTEVEDOLTASNKEQYAOVLVVG I 560
KVPKYEGRAGFAVIKLTNSLDITAKTKLLNDSLRLNLP 600
610 620 630 640
SYAMPLFVKFVDEIKMTONLIK. 624

Fig. 87

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mtFATP coding only.DNA

10 20 30 40
GTGTCCGATTACTACGGCGGGCGCACACACAACGGTCAGGC 40
TGATCGACCTGGCAACTCGGATGCCGCGAGTGTGGCGGA 80
CACGCCGGTGATTGTGCGTGGGGCAATGACCGGGCTGCTG 120
GCCCCGGCGAATTCCAAGGCGTCGATCGGCACGGTGTTC 160
AGGACCGGGCGCTCGCTACGGTGACCGAGTCTTCCTGAA 200

210 220 230 240
ATTCGGCGATCAGCAGCTGACCTACCGCGACGCTAACGCC 240
ACCGCCAACCGGTACGCCGCGGTGTTGGCCGCCCGCGCG 280
TCGGCCCCGGCGACGTCGTTGGCATCATGTTGCGTAACTC 320
ACCCAGCACAGTCTTGGCGATGCTGGCCACGGTCAAGTGC 360
GGCGCTATCGCCGGCATGCTCAACTACCACCAGCGCGCG 400

410 420 430 440
AGGTGTTGGCGCACAGCCTGGGTCTGCTGGACGCGAAGGT 440
ACTGATCGCAGAGTCCGACTTGGTCAGCGCCGTCGCCGAA 480
TGCGGCGCCTCGCGCGGCCGGGTAGCGGGCGACGTGCTGA 520
CCGTCGAGGACGTGGAGCGATTGCCACAACGGCGCCCCGC 560
CACCAACCCGGCGTCGGCGTCGGCGGTGCAAGCCAAAGAC 600

610 620 630 640
ACCGCGTTCTACATCTTCACCTCGGGCACCACCGGATTTT 640
CCAAGGCCAGTGTTCATGACGCATCATCGGTGGCTGCGGGC 680
GCTGGCCGTCTTCGGAGGGATGGGGCTGCGGCTGAAGGGT 720
TCCGACACGCTCTACAGCTGCCTGCCGCTGTACCACAACA 760
ACGCGTTAACGGTCGCGGTGTCGTGGTGATCAATTCTGG 800

810 820 830 840
GGCGACCCTGGCGCTGGGTAAAGTCGTTTTTCGGCGTCGCG 840
TTCTGGGATGAGGTGATTGCCAACC GGCGACGCGTTTCG 880
TCTACATCGGCGAAATCTGCCGTTATCTGCTCAACCAGCC 920
GGCCAAGCCGACCGACCGTGCCACCAGGTGCGGGTGATC 960
TGGGTAACGGGTGCGGCGGAGATCTGGGATGAGTTCA 1000

1010 1020 1030 1040
CCACCCGCTTCGGGGTCGCGCGGGTGTCGAGTTCTACGC 1040
CGCCAGCGAAGGCAACTCGGCTTTATCAACATCTTCAAC 1080
GTGCCAGGACCGCGGGGTATCGCCGATGCCGCTTGCTT 1120
TTGTGGAATACGACCTGGACACCGGCGATCCGCTGCGGGA 1160
TGCAGCGGGCGAGTGCCTCGGGTACCCGACGGTGAACCC 1200

Fig. 88A

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mtFATP coding only.DNA

1210	1220	1230	1240
GGCCTGTTGCTTAGCCGGGTCAACCGGCTGCAGCCGTTCC	1240		
ACGGCTACACCGACCCGGTTGCCAGCGAAAAGAAGTTGGT	1280		
GCGCAACGCTTTTCGAGATGGCGACTGTTGGTTCAACACC	1320		
GGTGACGTGATGAGCCCGCAGGGCATGGGCCATGCCGCCT	1360		
TCGTCGATCGGCTGGGCGACACCTTCCGCTGGAAGGGCGA	1400		
1410	1420	1430	1440
GAATGTCGCCACCACTCAGGTGGAAGCGGCACTGGCCTCC	1440		
GACCAGACCGTCGAGGAGTGCACGGTCTACGGCGTCCAGA	1480		
TTCCGCGCACCGGCGGGCGCGCCGGAATGGCCGCGATCAC	1520		
ACTGCGCGCTGGCGCCGAATTCGACGGCCAGGCGCTGGCC	1560		
CGAACGGTTTACGGTCACTTGCCCGGCTATGCACTTCCGC	1600		
1610	1620	1630	1640
TCTTTGTTCCGGGTAGTGGGGTCGCTGGCGCACACCACGAC	1640		
GTTCAAGAGTCGCAAGGTGGAGTTGCGCAACCAGGCCTAT	1680		
GGCGCCGACATCGAGGATCCGCTGTACGTACTGGCCGGCC	1720		
CGGACGAAGGATATGTGCCGTACTACGCCGAATACCCTGA	1760		
GGAGGTTTCGCTCGGAAGGCGACCGCAGGGCTAG	1794		

Fig. 88B

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mtFATP coding only.protein

10 20 30 40
MSDYYGGAHTTVRLIDLATRMPRVLADTPVIVRGAMTGLL 40
ARPNKASIGTVFODRAARYGDRVFLKFGDOOLTYRDANA 80
TANRYAAVLAARGVGPGDVVGIMLRNSPSTVLAMLATVKC 120
GAIAGMLNYHORGEVLAHSLGLLDAKVLIAESOLVSAVAE 160
CGASRGRVAGDVLTVEDVERFATTAPATNPASASAVOAKD 200
210 220 230 240
TAFYIFTSGTTGFPKASVMTHHRWLRALAVFGGMGLRLKG 240
SDTLYSCLPLYHNNALTVAVSSVINSGATLALGKSFSASR 280
FWDEVIANRATAFVYIGEICRYLLNOPAKPTDRAHQVRVI 320
CGNGLRPEIWDEFTTRFGVARVCEFYAASEGNSAFINIFN 360
VPRTAGVSPMPLAFVEYDLOTGDPLRDASGRVRRVPDGE 400
410 420 430 440
GLLLSRVNRLOPFDGYTDPVASEKKLVRNAFRDGCWFNT 440
GDVMSPOGMGHAAFVORLGOTFRWKGENVATTOVEAALAS 480
DQTVEECTVYGVOIPRTGGRAGMAAITLRAGAEFDGQALA 520
RTVYGHLPGYALPLFVRVVGSLAHTTTFKSRKVELRNOAY 560
GADIEDPLYVLAGPDEGYVPYYAEYPEEVSLGRRPOG. 598

Fig. 89

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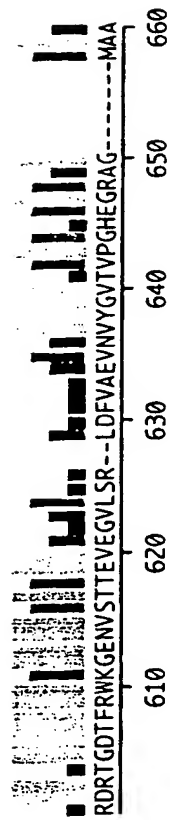
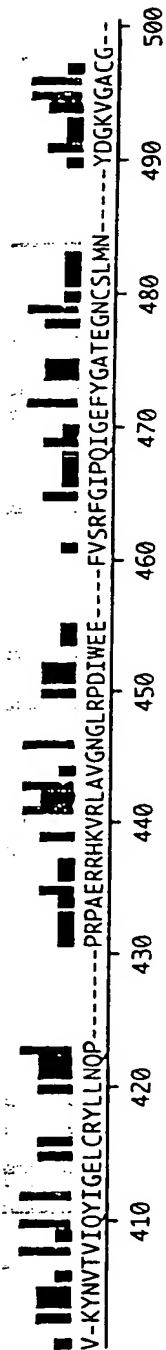
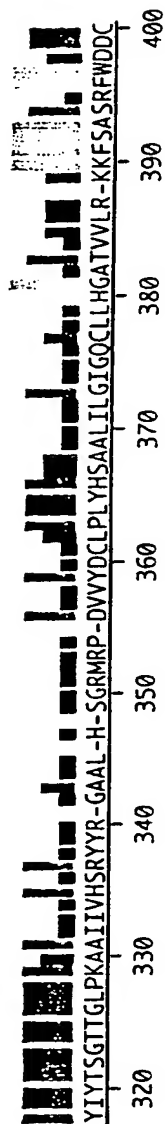


Figure 90

11

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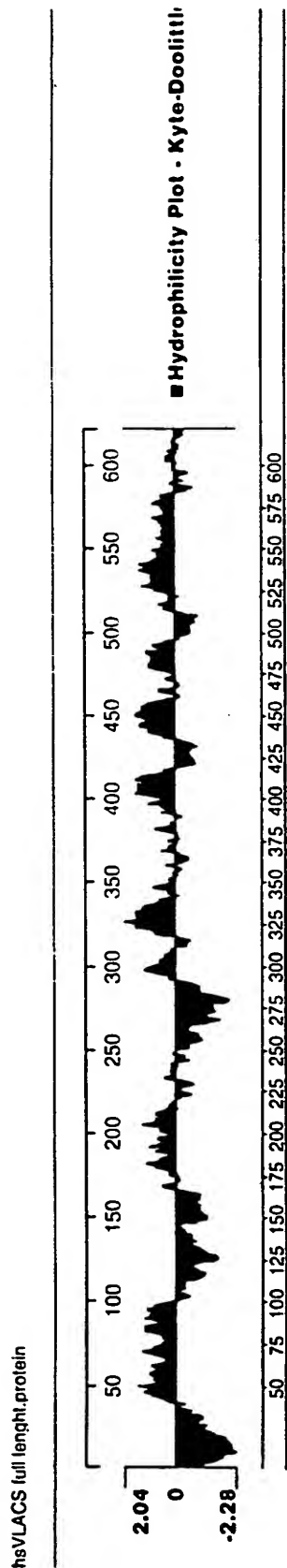


Figure 91

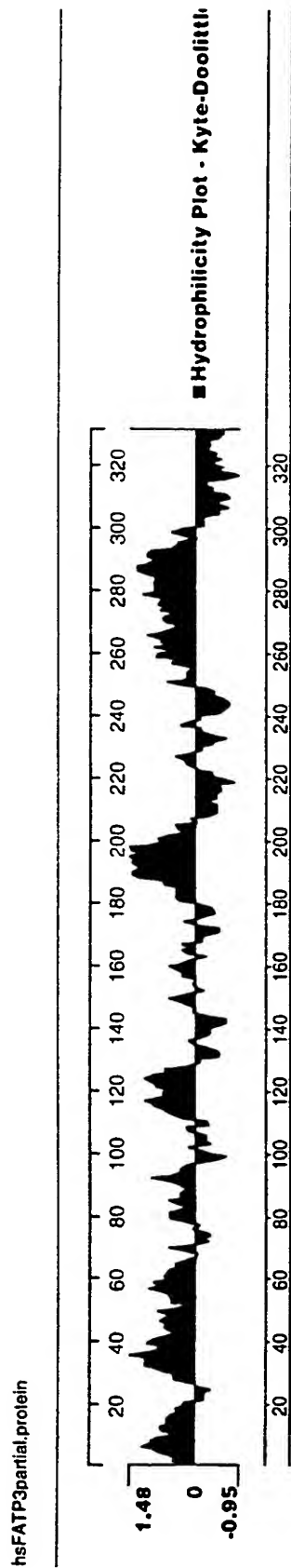
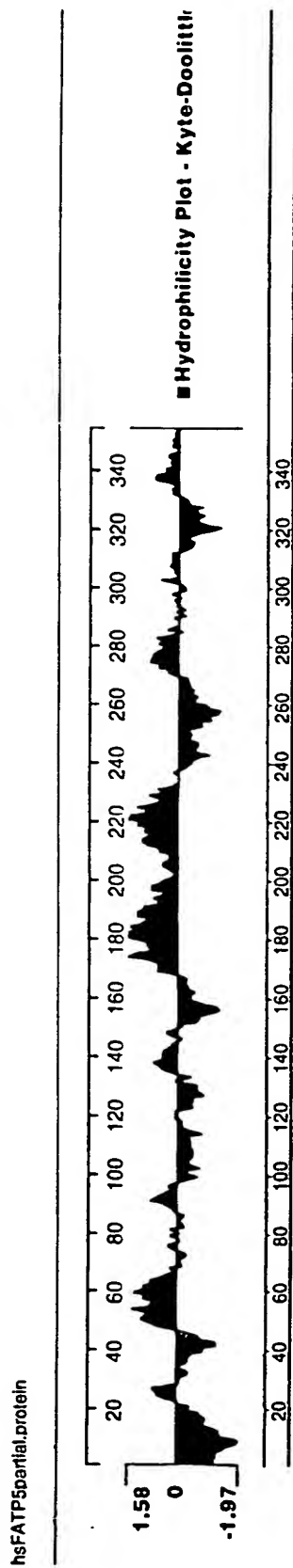


Figure 92



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Figure 93

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hsFATP3

1 cga ccc acg cgt ccg ggg atg ttt gcg agc ggc tgg aac cag acg gtg ccg ata gag gaa
1 M F A S G W N Q T V P I E E

61 gcg ggc tcc atg gct gcc ctc ctg ctg ctg ccc ctg ctg ctg ttg cta ccg ctg ctg ctg
15 A G S M A A L L L L P L L L L L P L L L L

121 ctg ctg aag cta cac ctc tgg ccg cag ttg cgc tgg ctt ccg gcg gac ttg gcc ttt gcg
35 L L K L H L W P Q L R W L P A D L A F A

181 gtg cga gct ctg tgc tgc aaa agg gct ctt cga gct cgc gcc ctg gcc gcg gct gcc gcc
55 V R A L C C K R A L R A R A L A A A A A

241 gac ccg gaa ggt ccc gag ggg ggc tgc agc ctg gcc tgg cgc ctc gcg gaa ctg gcc cag
75 D P E G P E G G C S L A W R L A E L A Q

301 cag cgc gcc gcg cac acc ttt ctc att cac ggc tgc cgg cgc ttt agc tac tca gag gcg
95 Q R A A H T F L I H G S R R F S Y S E A

361 gag cgc gag agt aac agg gct gca cgc gcc ttc cta cgt gcg cta ggc tgg gac tgg gga
115 E R E S N R A A R A F L R A L G W D W G

421 ccc gac ggc ggc gac agc ggc gag ggg agc gct gga gaa ggc gag cgg gca gcg ccg gga
135 P D G G D S G E G S A G E G E R A A P G

481 gcc gga gat gca gcg gcc gga agc ggc gcg gag ttt gcc gga ggg gac ggt gcc gcc aga
155 A G D A A A G S G A E F A G G D G A A R

541 ggt gga gga gag ccc gcc gcc cct ctg tca cct gga gca act gtg gcg ctg ctc ctc ccc
175 G G G E P A A P L S P G A T V A L L L P

601 gct ggc cca gag ttt ctg tgg ctc tgg ttc ggg ctg gcc aag gcc ggc ctg cgc act gcc
195 A G P E F L W L W F G L A K A G L R T A

661 ttt gtg ccc acc gcc ctg cgc cgg ggc ccc ctg ctg cac tgc ctc cgc agc tgc ggc gcg
215 F V P T A L R R G F L L H C L R S C G A

721 cgc gcg ctg gtg ctg gcg cca gag ttt ctg gag tcc ctg gag ccg gac ctg ccc gcc ctg
235 R A L V L A P E F L E S L E P D L P A L

781 aga gcc atg ggg ctc cac ctg tgg gct gca ggc cca gga acc cac cct gct gga att agc
255 R A M G L H L W A A G P G T H P A G I S

841 gat ttg ctg gct gaa gtg tcc gct gaa gtg gat ggg cca gtg cca gga tac ctc tct tcc
275 D L L A E V S A E V D G P V P G Y L S S

901 ccc cag agc ata aca gac acg tgc ctg tac atc ttc acc tct ggc acc acg ggc ctc ccc
295 P Q S I T D T C L Y I F T S G T T G L P

961 aag gct gct cgg atc agt cat ctg aag atc ctg caa tgc cag ggc ttc tat cag ctg tgt
315 K A A R I S H L K I L Q C Q G F Y Q L C

1021 ggt gtc cac cag gaa gat gtg atc tac ctc gcc ctc cca ctc tac cac atg tcc ggt tcc
335 G V H Q E D V I Y L A L P L Y H M S G S

1081 ctg ctg ggc atc gtg ggc tgc atg ggc att ggg gcc aca gtg gtg ctg aaa tcc aag ttc
355 L L G I V G C M G I G A T V V L K S K F

1141 tgc gct ggt cag ttc tgg gaa gat tgc cag cag cac agg gtg acg gtg ttc cag tac att
375 S A G Q F W E D C Q Q H R V T V F Q Y I

1201 ggg gag ctg tgc cga tac ctt gtc aac cag ccc ccg agc aag gca gaa cgt ggc cat aag
395 G E L C R Y L V N Q P P S K A E R G H K

Figure 94A

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1261 gtc cgg ctg gca gtg ggc agc ggg ctg cgc cca gat acc tgg gag cgt ttt gtg cgg cgc
415 V R L A V G S G L R F D T W E R F V R R

1321 ttc ggg ccc ctg cag gtg ctg gag aca tat gga ctg aca gag ggc aac gtg gcc acc atc
435 F G P L Q V L E T Y G L T E G N V A T I

1381 aac tac aca gga cag cgg ggc gct gtg ggg cgt gct tcc tgg ctt tac aag cat atc ttc
455 N Y T G Q R G A V G R A S W L Y K H I F

1441 ccc ttc tcc ttg att cgc tat gat gtc acc aca gga gag cca att cgg gac ccc cag ggg
475 P F S L I R Y D V T T G E P I R D P Q G

1501 cac tgt atg gcc aca tct cca ggt gag cca ggg ctg ctg gtg gcc ccg gta agc cag cag
495 H C M A T S P G E F G L L V A P V S Q Q

1561 tcc cca ttc ctg ggc tat gct ggc ggg cca gag ctg gcc cag ggg aag ttg cta aag gat
515 S P F L G Y A G G P E L A Q G K L L K D

1621 gtc ttc cgg cct ggg gat gtt ttc ttc aac act ggg gac ctg ctg gtc tgc gat gac caa
535 V F R P G D V F F N T G D L L V C D D Q

1681 ggt ttt ctg cgc ttc cat gat cgt act gga gac acc ttc agg tgg aag ggg gag aat gtg
555 G F L R F H D R T G D T F R W K G E N V

1741 gcc aca acc gag gtg gca gag gtc ttc gag gcc cta gat ttt ctt cag gag gtg aac gtc
575 A T T E V A E V F E A L D F L Q E V N V

1801 tat gga gtc act gtg cca ggg cat gaa ggc agg gct gga atg gca gcc cta gtt ctg cgt
595 Y G V T V F G H E G R A G M A A L V L R

1861 ccc ccc cac gct ttg gac ctt atg cag ctg tac acc cac gtg tct gag aac ttg cca cct
615 F P H A L D L M Q L Y T H V S E N L P P

1921 tat gcc cgg ccc cga ttc ctg agg ctg cag gag tct ttg gcc acc aca gag acc ttc aaa
635 Y A R P R F L R L Q E S L A T T E T F K

1981 cag cag aaa gtt cgg atg gca aat gag ggc ttc gac ccc agc acc ctg tct gac cca ctg
655 Q Q K V R M A N E G F D P S T L S D P L

2041 tac gtt ctg gac cag gct gta ggt gcc tac ctg ccc ctg aca act gcc cgg tac agc gcc
675 Y V L D Q A V G A Y L P L T T A R Y S A

2101 ctg ctg gca gga aac ctt cga atc tga gaa ctt cca cac ctg agg cac ctg aga gag gaa
695 L L A G N L R I

2161 ctc tgt

Figure 94B

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NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA,
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: FATTY ACID TRANSPORT PROTEINS

(57) Abstract: A family of fatty acid transport proteins (FATPs) mediate transport of long chain fatty acids (LCFAs) across cell membranes into cells. These proteins exhibit different expression patterns among the organs of mammals. Nucleic acids encoding FATPs of this family, vectors comprising these nucleic acids, as well as the production of FATP proteins in host cells are described. Also described are methods to test FATPs for fatty acid transport function, and methods to identify inhibitors or enhancers of transport function. The altering of LCFA uptake by administering to the mammal an inhibitor or enhancer of FATP transport function of a FATP in the small intestine can decrease or increase calories available as fats, and can decrease or increase circulating fatty acids. The organ specificity of FATP distribution can be exploited in methods to direct drugs, diagnostic indicators and so forth to an organ such as the heart.

WO 99/36537 A3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/00182

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/12 C12N9/00 C12N15/62 G01N33/68 C12Q1/68
C07K16/40

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	DATABASE EMBL - EMHUM1 [Online] Entry/Acc.no. D88308, 1 December 1997 (1997-12-01) KAMIJO, K.: "Homo sapiens mRNA for very-long-chain acyl-CoA synthase, complete cds." XP002107854	1-29
Y	the whole document	59-67, 89-94, 98-104, 108,112, 116,118, 120,158, 162, 167-173, 204
	---	-/--

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

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International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	<p>DATABASE EMBL - EMBEST1 [Online] Entry/Acc.no. Aa581592, 11 September 1997 (1997-09-11) STRAUSBERG, R.: "nc84e10.s1 NCI CGAP GC1 Homo sapiens cDNA clone IMAGE:797514." XP002116951 the whole document</p> <p>---</p>	<p>3,5,6,8, 9,14,21, 22</p>
X	<p>DATABASE EMBL - EMBEST25 [Online] Entry HSAA69992, Acc.no. AA469992, 21 June 1997 (1997-06-21) HILLIER, L. ET AL.: "zul0c02.r1 Soares testis NHT Homo sapiens cDNA clone 731426 5'." XP002116952 the whole document</p> <p>---</p>	<p>3,5,6,8, 9,14,21, 22, 185-187</p>
Y	<p>the whole document</p> <p>---</p>	<p>140,142, 144,146, 148,150</p>
X	<p>DATABASE EMBL - EMBEST1 [Online] Entry/Acc.no. Aa614135, 13 October 1997 (1997-10-13) STRAUSBERG, R.: "no82f09.s1 NCI CGAP AA1 Homo sapiens cDNA clone IMAGE:1113353 similar to TR:G563829 G563829 FATTY ACID TRANSPORT PROTEIN." XP002116953 the whole document</p> <p>---</p>	<p>3,5,6,8, 9,14,21, 22, 185-187</p>
Y	<p>the whole document</p> <p>---</p>	<p>1,2,4,7, 10-13, 15-20, 23-29, 77-85</p>
X	<p>DATABASE EMBL - EMBEST14 [Online] Entry HS808343, Acc.no.W48808, 30 May 1996 (1996-05-30) HILLIER, L. ET AL.: "zc44h06.r1 Soares senescent fibroblasts NbHSF Homo sapiens cDNA clone 325211 5' similar to PIR:A55093 A55093 fatty acid transport protein precursor - mouse." XP002116954 the whole document</p> <p>---</p>	<p>32,34, 35,37, 38,43, 50,51</p>
Y	<p>the whole document</p> <p>---</p>	<p>30,31, 33,36, 39-42, 44-49, 52-58</p>
	<p>---</p> <p>-/--</p>	

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/00182

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL - EMBEST1 [Online] Entry/Acc.no. AA614445, 13 October 1997 (1997-10-13) STRAUSBERG, R.: "nn89d05.s1 NCI CGAP Br2 Homo sapiens cDNA clone IMAGE:1098345 similar to TR:G563829 G563829 FATTY ACID TRANSPORT PROTEIN." XP002116955</p>	<p>32,34, 35,37, 38,43, 50,51</p>
Y	<p>the whole document</p>	<p>30,31, 33,36, 39-42, 44-49, 52-58</p>
X	<p>--- UCHIYAMA, A. ET AL.: "Molecular cloning of cDNA encoding rat very long-chain acyl-CoA synthetase." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 271, no. 48, 29 November 1996 (1996-11-29), pages 30360-5, XP002107850</p>	<p>105,107, 109,111, 113,115, 141,143, 145,147, 151,174, 175</p>
Y	<p>the whole document</p>	<p>1,2,4,7, 10-13, 15-20, 23-29, 59-67, 77-85, 92-94, 98-100, 167-173, 204</p>
X	<p>--- HARMON, C.M. ET AL.: "Labelling of an 88 kDa adipocyte membrane protein by sulpho-N-succinimidyl long-chain fatty acid: inhibition of fatty acid transport." BIOCHEMICAL SOCIETY TRANSACTIONS, vol. 20, no. 4, November 1992 (1992-11), pages 811-3, XP002107851</p>	<p>105,107, 109,111, 113,115, 141,143, 145,147, 149,151</p>
Y	<p>the whole document</p>	<p>89-91, 101-104, 108,112, 116,118, 120,140, 142,144, 146,148, 150,158, 162</p>
	<p>--- -/--</p>	

INTERNATIONAL SEARCH REPORT

Internal Application No

PCT/US 99/00182

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 935 450 A (CONE JR CLARENCE D) 19 June 1990 (1990-06-19) column 26, line 27 - line 35; claim 34 ---	105,107, 109,111, 113,115, 140,143, 145,147, 149,151, 194,198, 199
X	DATABASE EMBL - EMBEST25 [Online] Entry HSAA70762, Acc.no.AA470762, 21 June 1997 (1997-06-21) STRAUSBERG, R.: "ne19b11.s1 NCI CGAP Co3 Homo sapiens cDNA clone IMAGE:881661." XP002116956 the whole document ---	32,34, 35,37, 38,43, 50,51
X	SCHAFFER ET AL: "Expression cloning and characterization of a novel adipocyte long chain fatty acid transport protein" CELL, vol. 79, 4 November 1994 (1994-11-04), pages 427-436, XP002081438 cited in the application the whole document ---	34
Y	the whole document ---	30,31, 33,36, 39-42, 44-49, 52-58
A	SCHAFFER ET AL: "Cloning and structure-function analysis of human heart fatty acid transport protein" CIRCULATION, vol. 96, no. 8-suppl., 9 November 1997 (1997-11-09), page 2031 XP002082456 the whole document ---	
A	GHOSH, B. ET AL.: "Molecular cloning and sequencing of human palmitoyl-CoA ligase and its tissue specific expression." MOLECULAR AND CELLULAR BIOCHEMISTRY, vol. 151, 1995, pages 77-81, XP002107852 see whole document, particularly fig.1 ---	
P,X	FITSCHER, B.A. ET AL.: "Tissue distribution and cDNA cloning of a human fatty acid transport protein (hsFATP4)." BIOCHIMICA ET BIOPHYSICA ACTA, vol. 1443, 22 December 1998 (1998-12-22), pages 381-5, XP002116950 figures 2,3 ---	1-29,34, 68-76, 176,177

-/--

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 99/00182

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	<p>HIRSCH, D. ET AL.: "A family of fatty acid transporters conserved from mycobacterium to man" PROC.NAT'L.ACAD.SCI.USA, vol. 95, July 1998 (1998-07), pages 8625-9, XP002107853 the whole document</p> <p style="text-align: center;">-----</p>	

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/ 00182

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely.
See FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically
3. ☐ Claims Nos.
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6 4(a)

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows.

See additional sheet.

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos..
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box 1.1

Although claims 198-203, and claims 194-197 in as far as they relate to in vivo use, are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box 1.1

Claims 105,107,109,111,113,115,141,143,145,147,149 and 151 could not be searched to completion due to insufficient characterization of the respective inhibitors in the description.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 59-67,167-175 completely, and 1-29,89-121,158, 160-162,194,195,197-199,204 partially

Human FATP2 protein, allelic variants thereof, nucleic acids encoding them and complements or portions thereof, nucleic acids which hybridize under stringent conditions to the aforementioned nucleic acids, vector comprising said nucleic acid, host cell comprising said vector, method of producing said peptide or a fusion protein comprising the amino acid sequence of said protein or a portion thereof using said host, method for detecting expression of said nucleic acid by hybridization, method for detecting allelic variants by amplification of nucleic acids from a sample and comparison to the provided nucleic acid sequence, antidody against said protein, method for detecting expression of said protein through the use of said antibody. Method for identifying an inhibitor of FATP2 activity comprising the use of the protein itself, a test animal, or a host cell expressing said protein, and inhibitors identified thereby.

2. Claims: 68-76,159,163-166,176-184 completely, and 1-29, 89-121,158,160-162,194,195,197-199,204 partially

Human FATP4 protein, allelic variants thereof, nucleic acids encoding them and complements or portions thereof, nucleic acids which hybridize under stringent conditions to the aforementioned nucleic acids, vector comprising said nucleic acid, host cell comprising said vector, method of producing said peptide or a fusion protein comprising the amino acid sequence of said protein or a portion thereof using said host, method for detecting expression of said nucleic acid by hybridization, method for detecting allelic variants by amplification of nucleic acids from a sample and comparison to the provided nucleic acid sequence, antidody against said protein, method for detecting expression of said protein through the use of said antibody. Method for identifying an inhibitor of FATP4 activity comprising the use of the protein itself, a test animal, or a host cell expressing said protein, and inhibitors identified thereby.

3. Claims: 77-88,122-157,185-193,196,200-202 completely, and 1-29,158,160-162,194,195,197-199,204 partially

Human FATP6 protein, allelic variants thereof, nucleic acids encoding them and complements or portions thereof, nucleic acids which hybridize under stringent conditions to the aforementioned nucleic acids, vector comprising said nucleic acid, host cell comprising said vector, method of producing said peptide or a fusion protein comprising the amino acid sequence of said protein or a portion thereof using said

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

host, method for detecting expression of said nucleic acid by hybridization, method for detecting allelic variants by amplification of nucleic acids from a sample and comparison to the provided nucleic acid sequence, antidody against said protein, method for detecting expression of said protein through the use of said antibody. Method for identifying an inhibitor of FATP6 activity comprising the use of the protein itself, a test animal, or a host cell expressing said protein, and inhibitors identified thereby.

4. Claims: 30-58,158,160-162 partially

Human FATP1 protein, allelic variants thereof, nucleic acids encoding them and complements or portions thereof, nucleic acids which hybridize under stringent conditions to the aforementioned nucleic acids, vector comprising said nucleic acid, host cell comprising said vector, method of producing said peptide or a fusion protein comprising the amino acid sequence of said protein or a portion thereof using said host.

5. Claims: 30-58,158,160-162 partially

Human FATP3 protein, allelic variants thereof, nucleic acids encoding them and complements or portions thereof, nucleic acids which hybridize under stringent conditions to the aforementioned nucleic acids, vector comprising said nucleic acid, host cell comprising said vector, method of producing said peptide or a fusion protein comprising the amino acid sequence of said protein or a portion thereof using said host.

6. Claims: 203 completely, and 30-58,158,160-162 partially

Human FATP5 protein, allelic variants thereof, nucleic acids encoding them and complements or portions thereof, nucleic acids which hybridize under stringent conditions to the aforementioned nucleic acids, vector comprising said nucleic acid, host cell comprising said vector, method of producing said peptide or a fusion protein comprising the amino acid sequence of said protein or a portion thereof using said host.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internal Application No

PCT/US 99/00182

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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